

PHYSIOLOGY

Handwritten Notes

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Name: _____

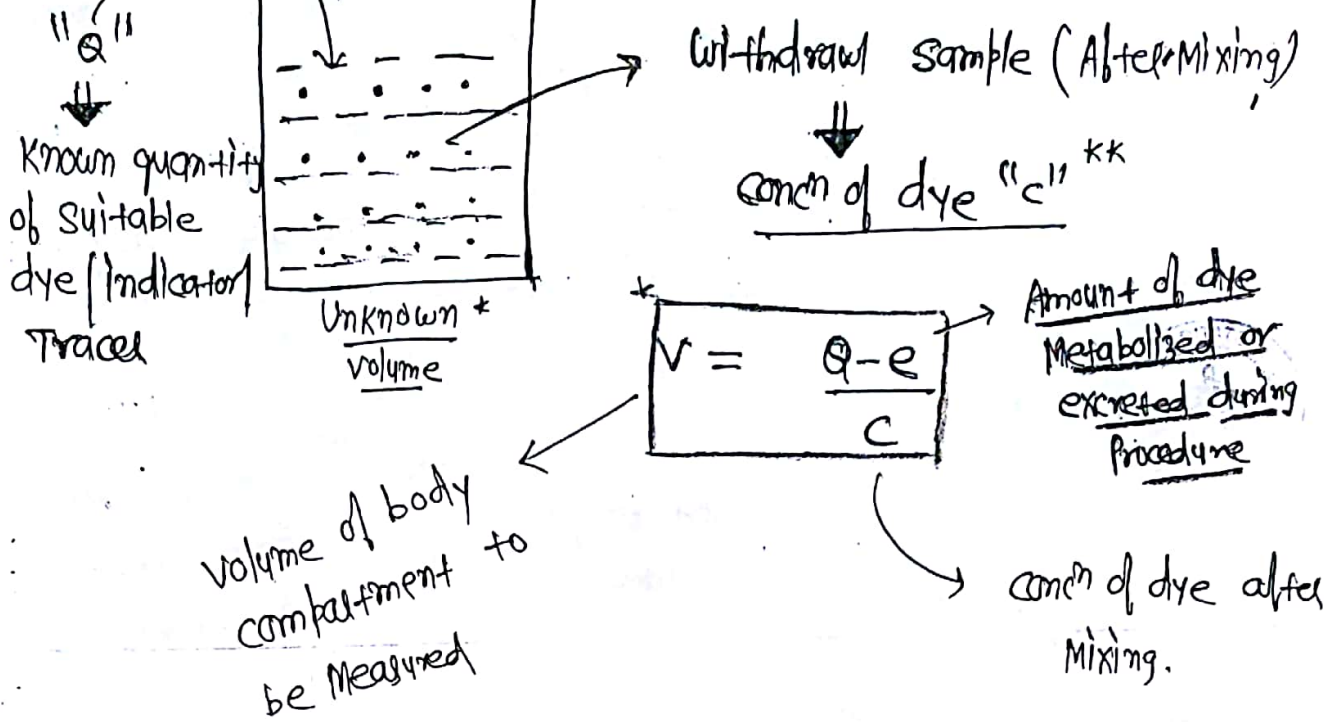
Subject: Physiology

All 2018 Handwritten notes by **MBBS Help**

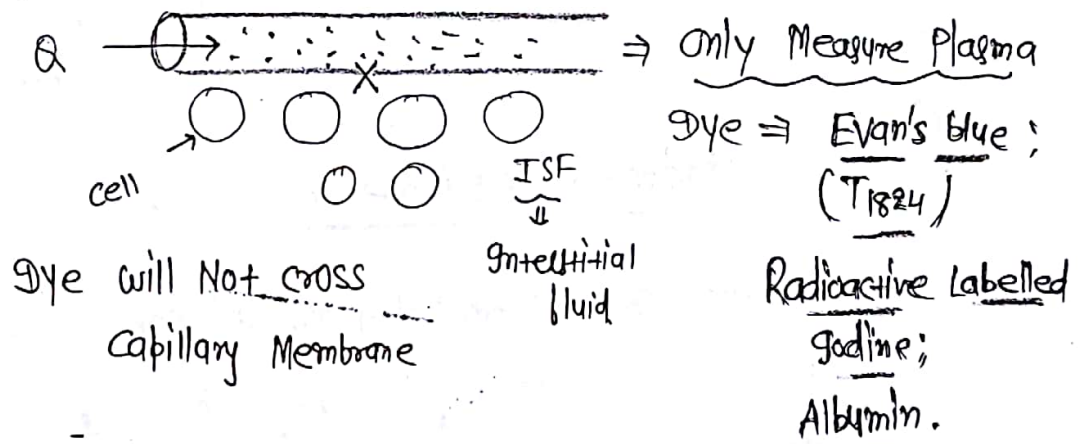


PHYSIOLOGY

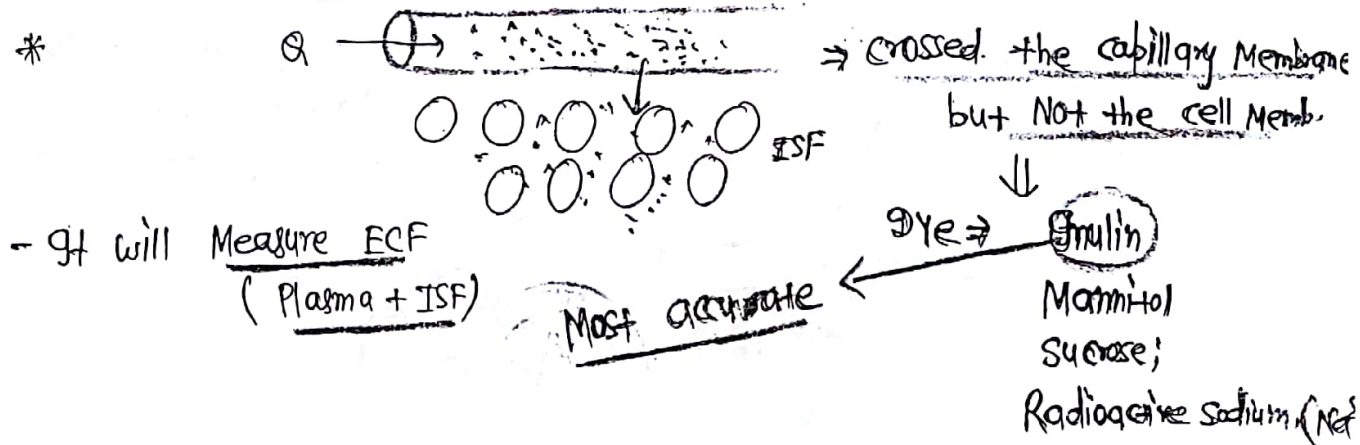
①



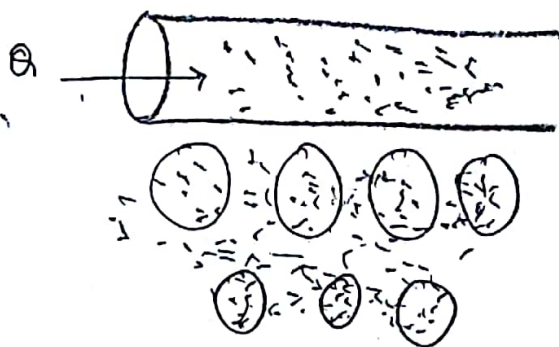
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*



① *



Cross Capillary Membr &
Cell Membr.



Measures TBW*



dye \Rightarrow D_{20}

Tritium oxide;
Amino Pyrine;
Anti-pyrine aa

Most frequently
used

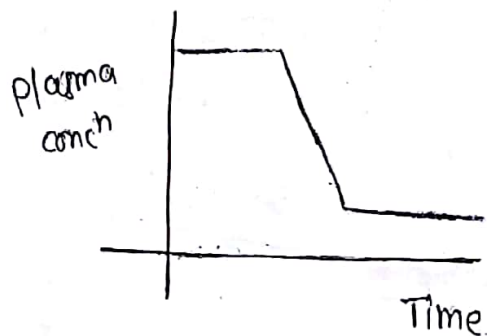
* GCF Measurement \Rightarrow TBW - ECF
(D_{20} - Inulin)

GCF Measurement \Rightarrow ECF - plasma
(Inulin Evan's blue)

Indirect estimation

Q. 15

We want to determine ECF volume, we take logms
of Inulin; After equilibrium; pl. Inulin 50mg/100ml; during
the procedure not excreted; ECF volume = ?



$$V = \frac{10,000 - 1000}{500} = 18 \text{ Litre}$$

Q. Q

"xyz" dye \rightarrow Plasma volume Measure



"ABC" dye \Rightarrow Diffuses out of tissue capillary

Pl. volume Measurement \bar{c} dye "ABC".

a) Same as \bar{c} "xyz"

b) Falsely high

c) Falsely Low

$$V = \frac{Q - e}{\bar{c}}$$

$$\uparrow \text{es } V = \frac{Q}{\bar{c} \downarrow \text{es}}$$

* Measurement of solute concn

MOLE \Rightarrow Gram Molecular wt.

32 gm of O_2 = 1 mole of O_2 .

58.5 gm of NaCl = 1 mole of NaCl.

67,000 gm of Albumin = 1 mole of albumin.

$$1 \text{ mole} = \underline{6.023 \times 10^{23} \text{ Molecules}}$$

\hookrightarrow Avogadro No.

$$\underline{\text{Millimole}} = \frac{1}{1000} \text{ th of Mole}$$

OS MOLE \Rightarrow

$$\underline{1 \text{ Osmol}} = \frac{1 \text{ Mole}}{\text{No. of Freely moving particles liberated in solution}}$$

* 1 Osmol of NaCl = $\frac{1 \text{ mole of NaCl}}{2}$

1 mole of NaCl = 2 osm

1 mole of KCl = 2 osm

1 mole of CaCl_2 = 3 osm

1 mole of Na_2SO_4 = 3 osm

1 mole of $\text{C}_6\text{H}_{12}\text{O}_6$ = 1 osm

1 mole of Urea = 1 osm

1 mole of Albumin = 1 osm

* Milliosmol $\Rightarrow \frac{1}{1000}$ th of osmol

OSMOLARITY

- No. of osmols of solute per Litre of solution.
- affected by - Temp.

OSMOLALITY

- No. of osmols of solute per kg of solvent.
- Not affected by temp, so, better to use

Q. (N) Plasma osmolality $\Rightarrow 280-290 \text{ mosm/Litre}$

* if there is \uparrow Plasma osmolality \Rightarrow eg \Rightarrow Sweating (Hypo-tonic)

ADH - Thirst
Mechn for Regulation
of Plasma
osmolality & the Nat Levels

\uparrow stly \uparrow in ADH & Thirst comes later
b/c Max contribution

Stimulates osmoreceptors

(Located @ Ant. hypothalamus)

Supraoptic (for Plasma osmolality by 5 mosm/L)
(TADH)

Lateral hypothalamus

\uparrow Plasma osmolality

Q. Maxm contribution to plasma osmolality \Rightarrow (3)

a) ~~Sodium~~ & its associated anions \Rightarrow 270 mosmol

b) Glucose \Rightarrow 5 mosmol

c) Urea \Rightarrow 5 mosmol

d) Pl. proteins \Rightarrow 2 mosmol*

↳ Least contribution

e) Remaining ions \Rightarrow 8 mosmol

290 mosmols

* (N) Plasma proteins \Rightarrow 6-8 gm/dl } Fairly high concn.

(N) Albumin proteins \Rightarrow 3.5-5.0 gm/dl }
(35-50 gm/L)

67,000 gm of Albumin = 1 mole of Albumin = 1 mosm of Albumin

50 gm of Albumin = $\frac{1}{67,000} \times 50$ moles of Albumin = 0.00075 moles
= 0.00075 osmoles

* $\left\{ \begin{array}{l} \text{No. of Moles or} \\ \text{osmoles of protein} \end{array} \right. = \frac{\text{Concn in gm/Litre}}{M_w}$

Q. Plasma proteins contributes only 2 mosmol to plasma osmolality \Rightarrow

a) high molar concn; high M_w

b) Low molar concn; Low M_w

c) High molar concn, Low M_w

~~d) Low molar concn; high M_w .~~

Q.Q. Plasma proteins contributes only 2 mOsm/L to plasma osmolality; b/c of \rightarrow

~~a)~~ high concn; high Mw.

b) Low concn; Low Mw

c) High concn; Low Mw

d) Low concn; high Mw

Proteins — High concn (^{gram/litre} g/L)
but b/c of high Mw

$\downarrow\downarrow$

\downarrow Molal concn

\therefore Contribution to Plasma osmolality also less.

*

How to Measure Plasma osmolality

$$\begin{aligned} \text{In mOsm/L} \Rightarrow & 2 [\text{Na}^+ + \text{K}^+] + 0.055 [\text{Glucose}] + 0.36 [\text{BUN}] \\ & \downarrow \quad \quad \quad \nearrow \frac{1}{18} \text{ Multiply } \frac{\text{mg/dl}}{\text{d. weight}} \\ & \text{mmol/L or meq/L} \quad \quad \quad (\text{mmol/L}) \text{ mg/dl} \\ & \quad \quad \quad \downarrow \\ & 2 [\text{Na}^+] \quad \quad \quad (\text{mmol/L}) \text{ mg/dl.} \end{aligned}$$

Q.

$$\text{Na}^+ = 140 \text{ meq/L}$$

$$\text{K}^+ = 5 \text{ meq/L}$$

$$\text{Glu} = 5 \text{ mOsmol/L}$$

$$\text{BUN} = 5 \text{ mOsmol/L}$$

Pl. osmolality = ?

$$\begin{aligned} & 2 [140 + 5] + 5 + 5 \\ & = 300 \text{ mOsmol/Litre} \end{aligned}$$

* Measurement of Plasma osmolality by freezing point depression (9)

⇒ 1 osmol of solute depress freezing point by 1.86°C

Q. Q. freezing point of soln \propto 1 mosmol of solute

a) 0°C ; b) $+1.86^{\circ}\text{C}$; ~~c) -1.86°C~~

* 1 mosmol of solute depresses freezing point by 0.00186°C

Q. Q. freezing point of plasma ⇒

a) 0°C

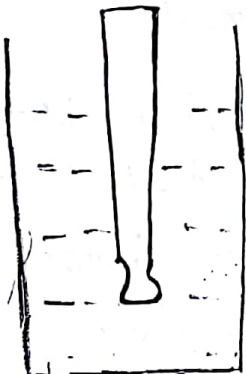
b) -1.86°C

~~c) -0.54°C~~

d) $+0.54^{\circ}\text{C}$

1 mosmol $\leftrightarrow -0.00186^{\circ}\text{C}$

290 — $\rightarrow 290 \times -0.00186^{\circ}\text{C}$
 $= -0.54^{\circ}\text{C}$



F.p.t.

$$\text{Pl. osmol (mosm/L)} = \frac{(\text{F.p.t.})^{\circ}\text{C}}{0.00186^{\circ}\text{C}}$$

⇒ More accurate to Measure the plasma osmolality.
 ↳ b/c we consider all things \oplus in plasma @ here

* (N) Pl. osm. by freezing point depression is higher than Pl. osmolality by using formula.

* (N) difference b/w two Method is $\leq 10 \text{ mosm/L}$

* if difference b/w two Methods $> 10 \text{ mosm/L}$



K/a " OSMOLAL GAP "

Q.Q.

Osmolal gap pr+. In all of the following except \Rightarrow

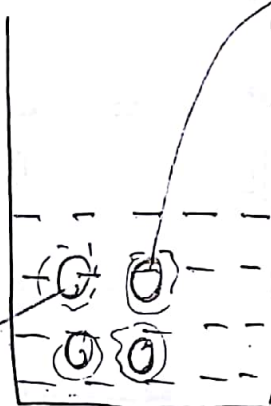
- a) Mannitol in Plasma
- b) Methanol in Plasma
- c) Ethylene glycol in Plasma
- d) Hyperglycemia

Osmolal gap is seen in the presence of "exogenous substance" in plasma.

Q.Q.

280 mosm/L

Into which solution have RBC been placed



a) ~~140 mmol Glucose = 140 mosm~~ Hypo-tonic

b) ~~280 mmol Glucose = 280 mosm~~ Iso-tonic

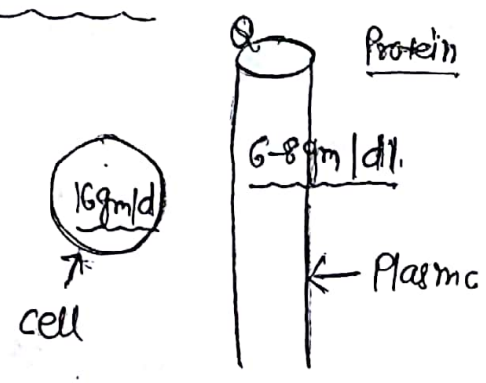
c) ~~140 mmol NaCl = 280 mosm~~ Iso-tonic

d) ~~280 mmol NaCl = 560 mosm~~ Hyper-tonic

*	ECF	ICF
Osmolality	290 mosm/L	290 mosm/L
Major cation	Na ⁺	K ⁺
Major Anion	Cl ⁻	Misc phosphates > HCO ₃ ⁻
Most osmotically active	Na ⁺	K ⁺
Major buffer	HCO ₃ ⁻	Proteins (∵ pK of proteins is close to Intracellular pH)
pH	7.35 - 7.45	7.1
H ⁺		Yes (as compare to ECF b/c of Metabolism in ICF)

Q. Which of the following is higher in ECF **

- a) Osmolality;
- b) proteins
- c) Phosphates
- ~~d) pH~~



OSMOTIC ADAPTATION

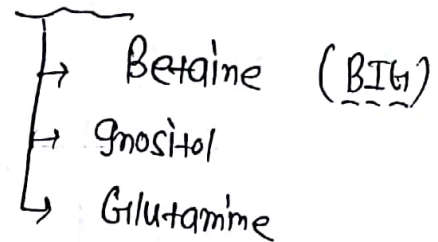
In chronic hypernatremia \Rightarrow

($> 24-48$ hrs)

Brain cells show osmotic adaptation.



i) \uparrow Intracellular synthesis of osmolytes



ii) Import of sodium

In chronic hyponatremia \Rightarrow

($> 24-48$ hrs)

brain cells show osmotic adaptation.

i) \downarrow Intracellular synthesis of osmolytes

ii) Export of K^+

* Rapid correction of chronic hyponatremia



Result in central Pontine Myelinolysis

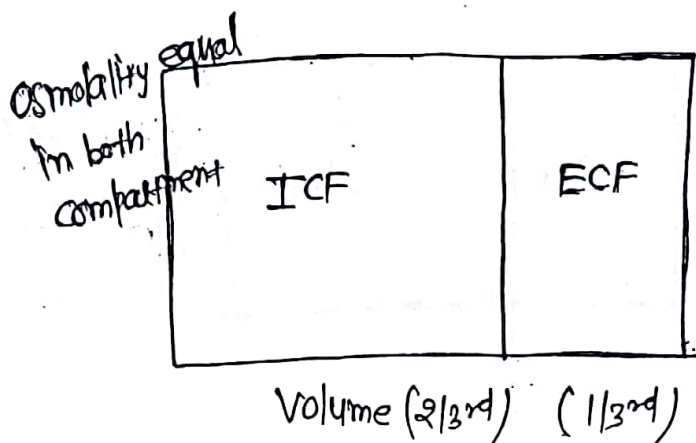
\hookrightarrow Result in death.

So; should Not correct Na^+ Rapidly; do; correction gradually

& Not More than 6 mmol/L/day . (on 1st day $\Rightarrow 6-8 \text{ mmol/L}$ correction done only & Later Na^+ gradually)

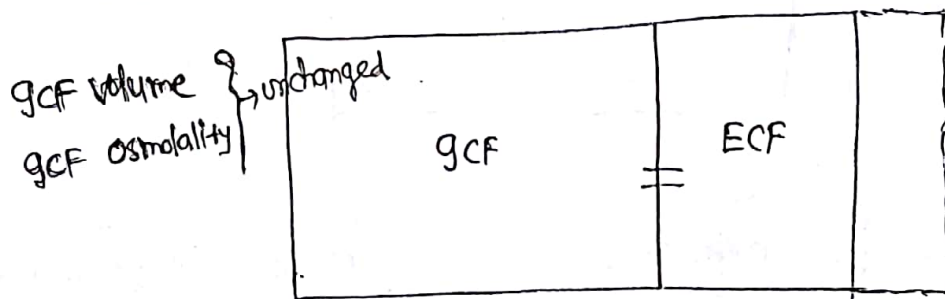
*

DARROW - YANNEY DIAGRAM (D-Y Diagram)



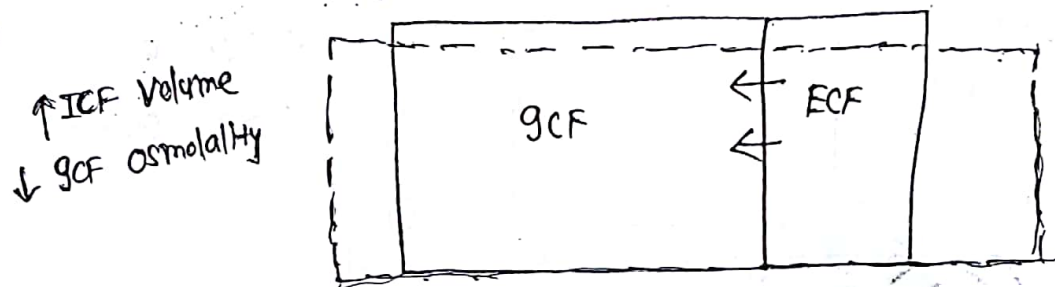
- ① Addition (Loss of Fluid is from ECF)
- ② ECF osmolality determines shift of fluid;
- ③ Shift of fluid will occur till ECF & ICF osmolality is same

* Addition of isotonic saline →



↑ in ECF volume
ECF osmolality
↳ Same

* Addition of Hypotonic saline →

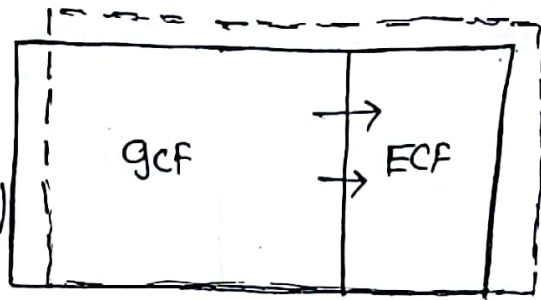


ECF volume ↑
↓ ECF osmolality

* Addition of Hypertonic saline \Rightarrow

\downarrow GCF volume

\uparrow GCF osmolality
(cellular dehydration)

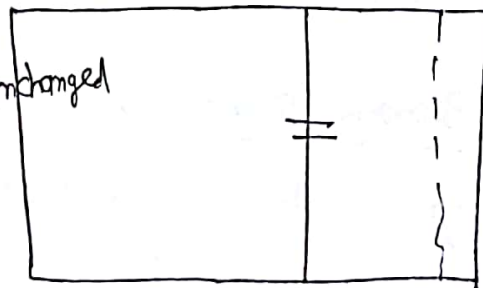


\uparrow ECF volume

\uparrow ECF osmolality

* Loss of iso-tonic fluids \Rightarrow eg \Rightarrow Hemorrhage;
Burns;
Initial stage of diarrhea & vomiting.
 \hookrightarrow iso osmotic dehydration

GCF volume } unchanged
GCF osmolality }

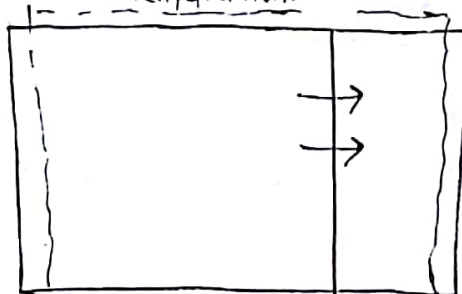


\downarrow ECF volume

ECF osmolality = unchanged

* Loss of hypotonic fluids \Rightarrow eg \Rightarrow Excessive sweating
Diabetes Insipidus
 \hookrightarrow hyperosmotic dehydration.

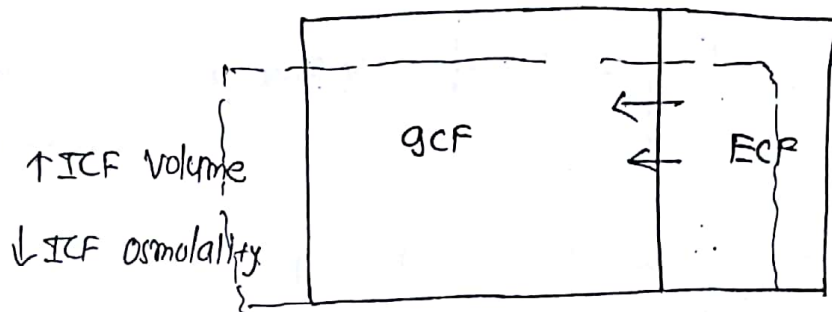
\downarrow ICF volume
 \uparrow ICF osmolality



\downarrow ECF volume

\uparrow ECF osmolality

* Loss of hypotonic fluids eg \Rightarrow Mineralocorticoid deficiency
 \downarrow Hypoosmotic dehydration \downarrow Addison's ds



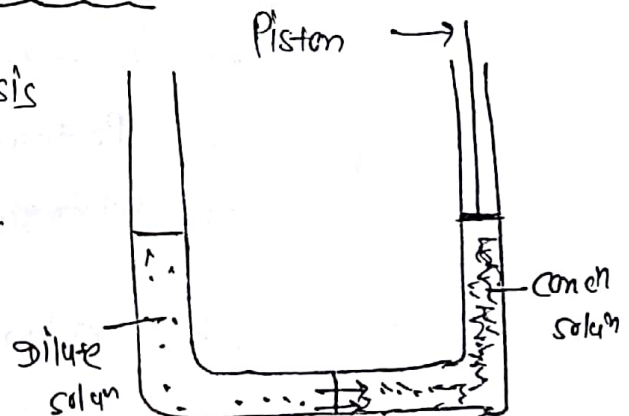
* OSMOTIC PRESSURE

- Pressure applied to stop osmosis

\downarrow
 K_{os} "osmotic-pressure"

* 1 mosm of solute

\downarrow exert osmotic pressure of 19.3 mm Hg



==

Osmotic pressure of plasma

\downarrow
 5500 mm of Hg ($290 \times 19.3 = 5597$)

\downarrow slightly lower than calculated b/c all solutes not contributed in osmotic pressure

* Colloid osmotic pressure (oncotic pressure)

→ osmotic pressure exerted by colloids (proteins)
 ↳ 25 - 28 mm of Hg

$$\text{Osmotic Pressure} = \frac{\text{No. of mols of Solute}}{\text{Volume}} \times 19.3 \times \text{Osmotic coefficient} \times \text{Reflection coefficient}$$

$$= 2 \times 19.3 \times 0.7$$

⇒

Q9 Which protein contributes Max^m to colloid os. pressure

- ☒ a) Albumin
- b) Globulin
- c) Prothrombin
- d) Fibrinogen

Q9 Why albumin contribute to colloid osmotic pressure?

- a) High concⁿ; high M_w
- b) Low concⁿ; Low M_w
- ☒ c) High concⁿ; Low M_w (compare to other proteins it has less M_w; while its concⁿ is high).
- d) Low concⁿ; High M_w

* Reflection coefficient ⇒ Freely permeable Solute : Reflection coefficient (σ) = 0.

Impermeable solute
 Reflection coefficient (σ) ↳ 1.0

cell Membrane

* Solute \bar{z} Reflection coefficient is zero



don't contribute to osmotic pressure



K/ay " ineffective osmoles "

eg \Rightarrow Alcohol

Glycerol

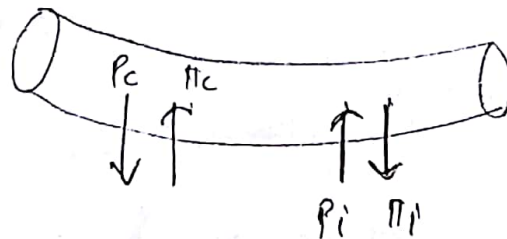
Urea \Rightarrow via facilitated diffusion

Glucose

* STARLING'S FORCES ON TISSUE CAPILLARY

PUSH = Hydrostatic Pressure

PULL = colloid osmotic Pressure



$P_c \Rightarrow$ capillary hydrostatic Pressure.

$\pi_c \Rightarrow$ capillary colloid osmotic Pressure

$P_i =$ Interstitial fluid hydrostatic pressure

$\pi_i =$ Interstitial colloid osmotic Pressure

$$\text{Net force} \Rightarrow P_c - \pi_c - P_i + \pi_i$$

$$\Rightarrow 35 - 25 - (-1) + 0$$

$$\Rightarrow +11 \text{ mm of Hg.}$$

$$P_c = 35 \text{ mm of Hg}$$

$$\pi_c = 25 \text{ mm of Hg}$$

$$P_i = -1 \text{ mm of Hg} \quad \left(\begin{array}{l} \text{ble of continuity} \\ \text{drainage into} \\ \text{lymphatics} \end{array} \right)$$

$$\pi_i = 0 \text{ mm of Hg}$$

Net pressure = 3 mm of Hg;

$$H_C = 28$$

$P_i = 7 \text{ mm of Hg}$

$$3 = 25 - \pi_c - 2 + 7$$

* Rate of tissue Fluid formation \propto Net pressure
 $(P_c - \pi_c - P_i + \pi_i)$
 $= K_b \underset{(3)}{P_c} - \underset{(4)}{\pi_c} - \underset{(5)}{P_i} + \underset{(6)}{\pi_i}$

$$= \frac{\text{Permeability}}{(1)} \times \frac{\text{Surface area}}{(2)}$$

* In cirrhosis
Nephrotic
syndrome

} Hypoalbuminemia
↓
↓ osmotic pressure
↓
↑ rate of tissue fluid formation
↓
Result in edema

Q. organ \bar{c} $\frac{\text{Maxim } P_c}{\text{L} \rightarrow \text{kidney}}$

Q. organ \bar{c} $\frac{\text{Maxim } K_b}{\text{L} \rightarrow \text{kidney}}$

Q. organ \bar{c} $\frac{\text{Maxim capillary permeability}}{\text{(Most permissible capillary)}}$
 $\text{L} \rightarrow \text{Liver}$

Hepatic capillary — Sinusoidal
Glomerulus capillary — Fenestrated

BLOOD VOLUME

B. volume = 8% of body wt.

Plasma = 5% of body wt.

cells = 3% of body wt.

$$\text{Blood volume} = \frac{100}{100 - \text{Hematocrit value}} \times \text{Pl. volume}$$

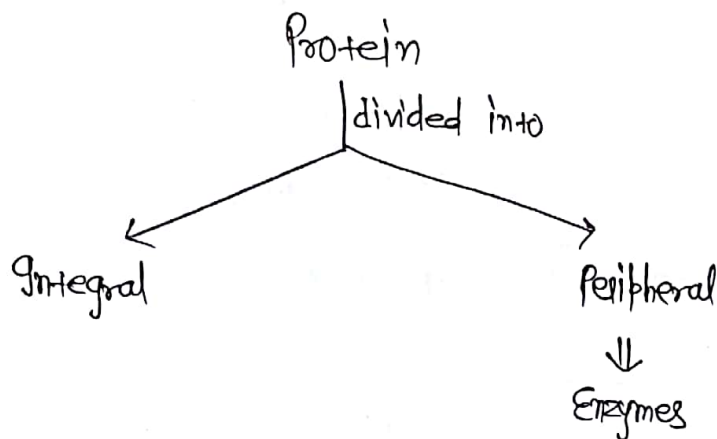
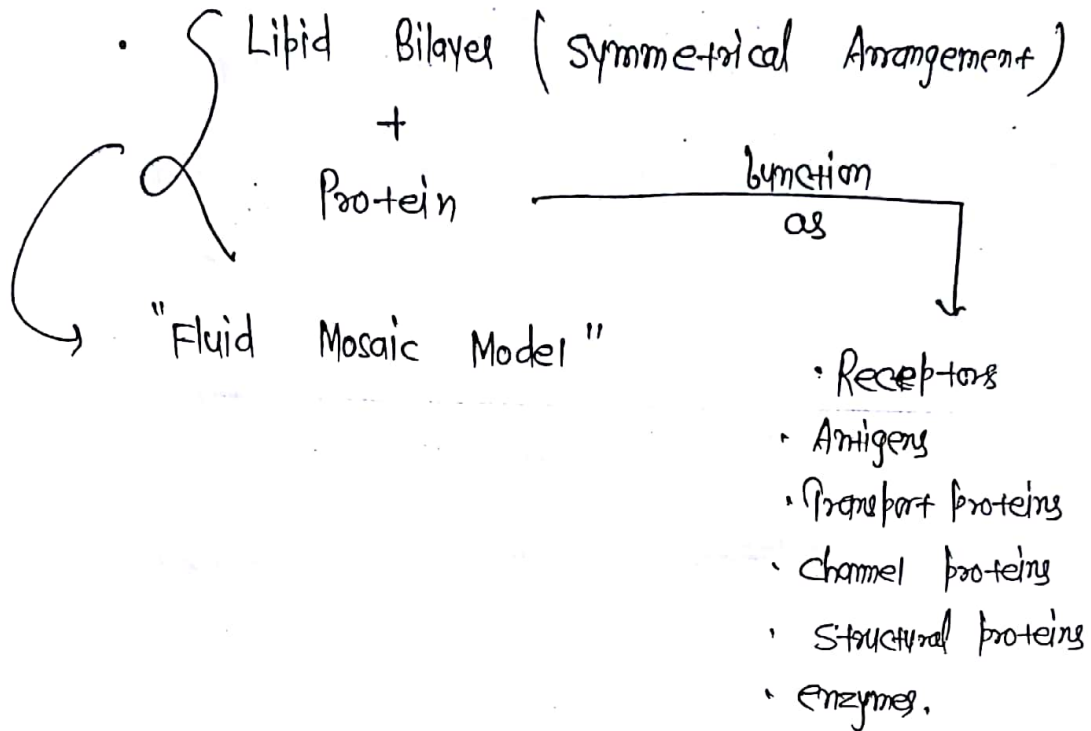
eg \Rightarrow Pl. volume = 3L

Hematocrit = 40

$$\text{Blood volume} = \frac{100}{100 - 40} \times 3 = 5 \text{ L}$$

CELL MEMBRANE

- Thickness = 7.5 nm
OR
75 Å



QA In terms of dry wt. of cell membrane; Maxm amount :-

Ratio (1:1)

⑨ Lipids

⑥ Proteins ⇒ 52% of dry wt. of cell membrane

* cell adhesion Molecules (CAMs) \Rightarrow

- cadherins
- Integrins
- Selectins
- Protein belonging to IgG Superfamily.

* TIGHT JUNCTIONS \Rightarrow formed by proteins

- \Downarrow
- occludins
 - claudins
 - JAMs (Functional Adhesion Molecule).

- Tight junctions all seen in \Rightarrow blw endothelial cells of cerebral capillaries

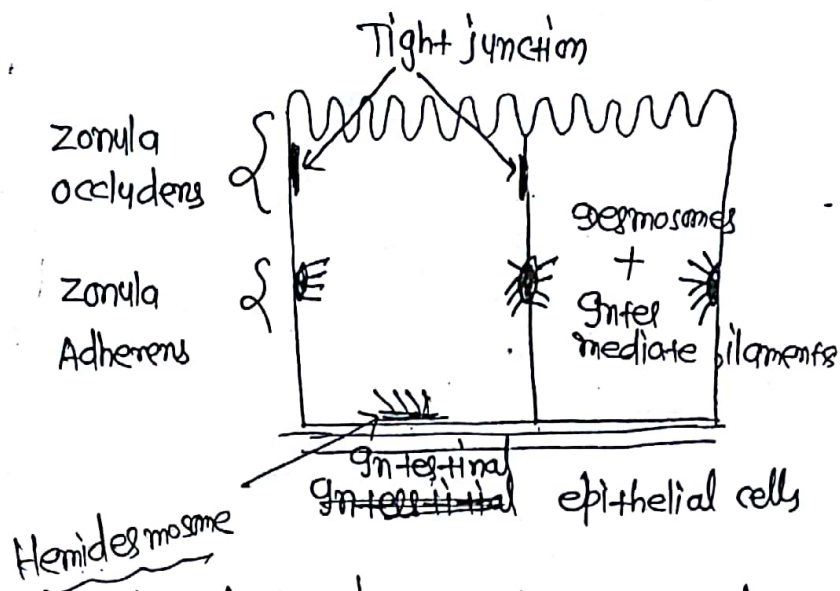
\downarrow BBB aa

\downarrow
Astrocyte induce formation of Tight junction.

- b/w ^{interstitial} ~~interstitial~~ epithelial cells
(Towards Luminal side)

- PCT

- 

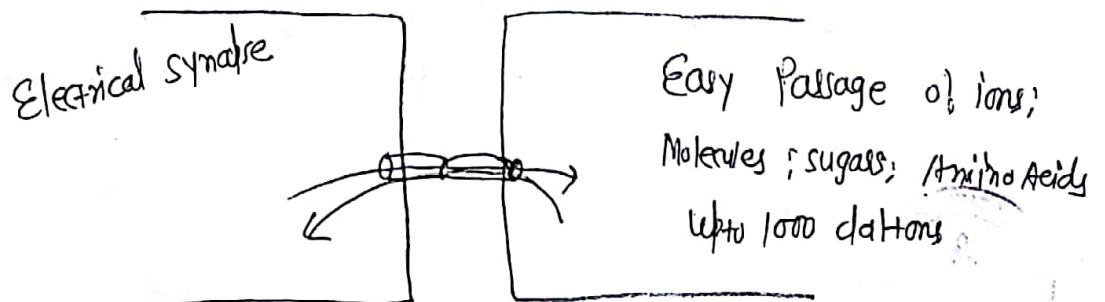
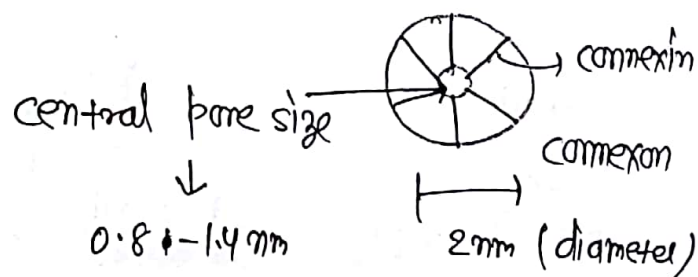


↳ helps in attachment to basement Membrane

GIAP JUNCTIONS ⇒ Made of Protein Connexons.



Each Connexion has 6 subunits
Klas "connexin"; which surround
central pore



Gap junction \rightarrow vs Intercellular junction

(N) Gap b/w Intercellular \Rightarrow 20nm
by Gap junction Reduces
by 3nm

eg \Rightarrow Retina
Cardiac Muscle (Heart - Functional Syncytium)
Single unit type of Smooth Muscle
(In wall of hollow viscera
eg \Rightarrow GI Muscle)

* If connexon Mutation

\rightarrow Charcot Marie tooth disease
(X-Linked disease).

TRANSPORT ACROSS CELL MEMBRANE

Passive

- "downhill transport"
- Along electrochemical gradient
- No energy Required
- eg \Rightarrow Simple diffusion
Facilitated diffusion
non-ionic "
channels

Active

- "Up hill" transport
- Against electrochemical gradient
- energy Required
- 10 Active
- 90 Active

Simple diffusion

- all Lipid soluble substance;
- Alcohols; steroids
- Respiratory gases

Fick's Law of diffusion \Rightarrow

$$J = - D A \frac{\Delta c}{\Delta x} \quad **$$

J = Net transport; D = Diffusion coefficient

A = Surface Area

Δc = concⁿ gradient.

Δx = thickness of Membrane

depends on

- Lipid solubility. (Most imp.)
- Molecular size/diameter
- M_w

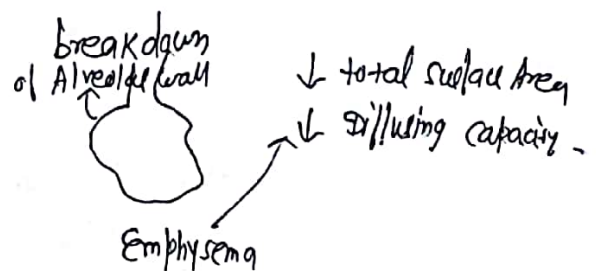
Diffusion coefficient \propto Lipid solubility

Molecular diameter $\sqrt{M_w}$


- if 2 Equal Lipid soluble substance; then Next imp. to determine diffusion coefficient \Rightarrow Molecular diameter

$J \propto A$ (surface Area)

In emphysema \Rightarrow



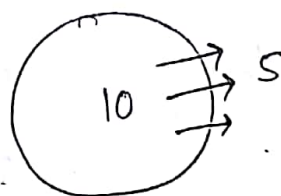
* In Pulmonary fibrosis \Rightarrow \downarrow Diffusing capacity.
b/c of \uparrow Thickness. (12)

$$J = - \frac{DA \Delta C}{\Delta x}$$


Shows direction of transport from higher concⁿ to Lower concⁿ.

Q. Q.

Membrane permeant substance



Intracellular concⁿ }
surface area } $\times 2$
thickness of Membrane }

the extracellular concⁿ \Rightarrow Same

Rate of transport \Rightarrow

a) $2x$; ~~b) $3x$~~ ; c) $\frac{1}{2}$; d) $\frac{1}{3}$

$$J = - \frac{DA \Delta C}{\Delta x}$$

Initially $\Rightarrow 10 - 5 \Rightarrow 5$
after double $\Rightarrow 20 - 5 \Rightarrow 15$
3-times res

} concⁿ gradient

FACILLIATED DIFFUSION

Carrier Mediated

i> Stereospecificity

L. Carrier protein is specific for a substance or structurally similar substance

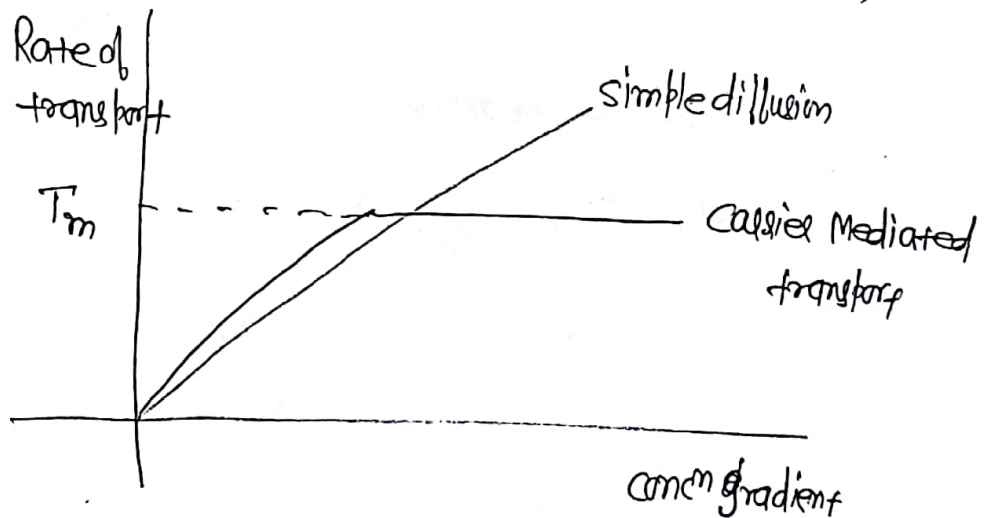
Glucose →
Galactose →
So, Galactose ⊕ ves Absorption of Glucose

GLUT

ii> Saturation Kinetics

Carrier protein — tend to get saturated

— T_m (transport Maxima)



eg: \Rightarrow GLUT \Rightarrow for Glucose;

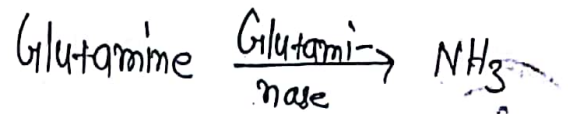
AA transporters

Urea transporters \Rightarrow In Kidney \Rightarrow UTA1, UTA2, UTA3, UTA4

RBC Vasa Recta \Rightarrow UTB

NON IONIC DIFFUSION

(13)

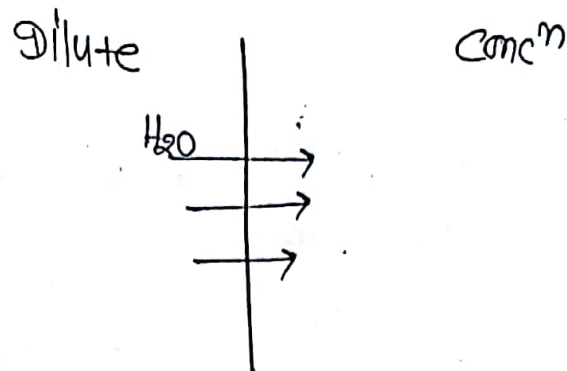


* NH_3 Moves from cell to Lumen & form NH_4^+ inside the Lumen.

- Secretion of NH_3 \rightarrow PCT (No H^+ in lumen to bind NH_3)
 \rightarrow collecting duct.
 - Non-ionic diffusion of NH_3 seen in \rightarrow collecting duct.
- eg \rightarrow
- Secretion of NH_3 by collecting duct cells;
 - Excretion of weak acids & weak bases by the kidney;
 - Absorption of weak acids (Salicylates) in stomach;
 - Absorption of bile acids in distal ileum.

OSMOSIS

- Movement of water from dilute to concⁿ solution;



Q.Q.

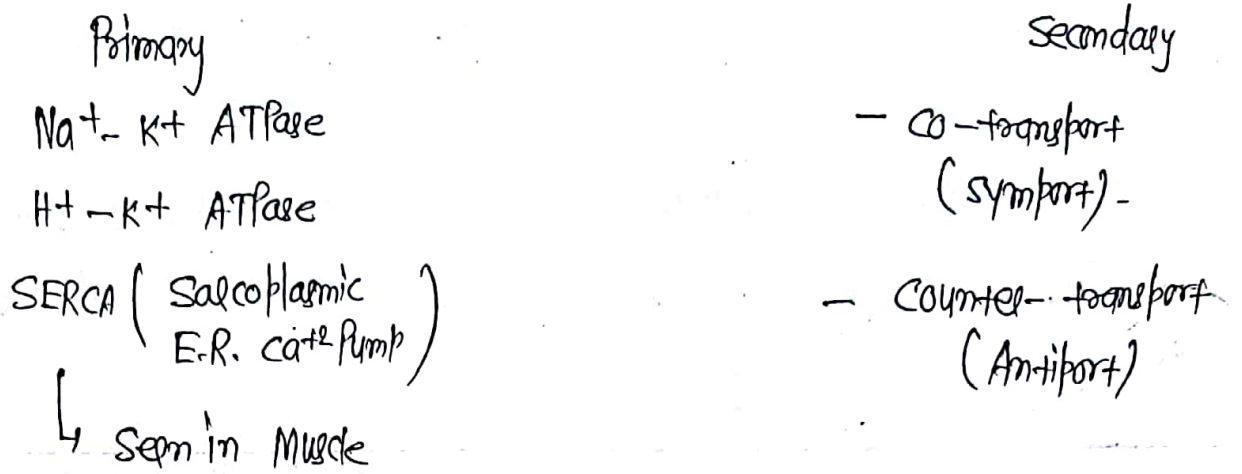
Movement of H₂O is by →

~~as~~ passive transport

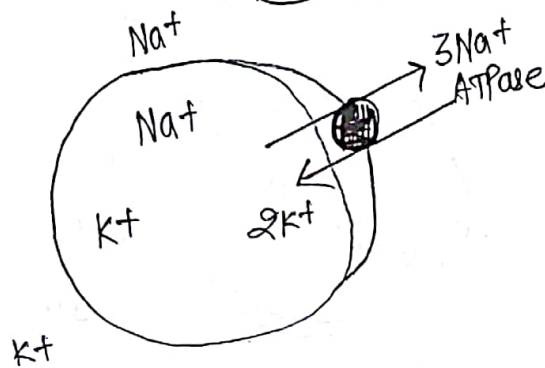
~~by~~ osmosis

ACTIVE TRANSPORT

(15)



Na⁺-K⁺ ATPase Pump



coupling Ratio

3:2

↳ b/c of two-stage

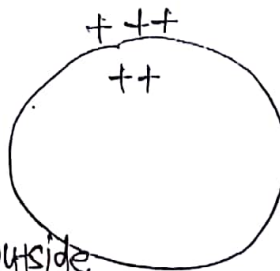
process (1stly sodium goes & then potassium comes)

— Electrogenic Pump

Net loss of one \oplus ve charge



Inside become \ominus ve w.r.t. outside



$$RMP = -90\text{mV};$$

$$\text{Contribution of } \text{Na}^+ - \text{K}^+ \text{ ATPase} = \underbrace{-4\text{mV}}_{\downarrow};$$

Not sufficient to Make RMP.

$\text{Na}^+ - \text{K}^+ \text{ ATPase}$ Pump utilize 25% of total energy of cell. (In Neurons \Rightarrow 75% of total energy of cell).



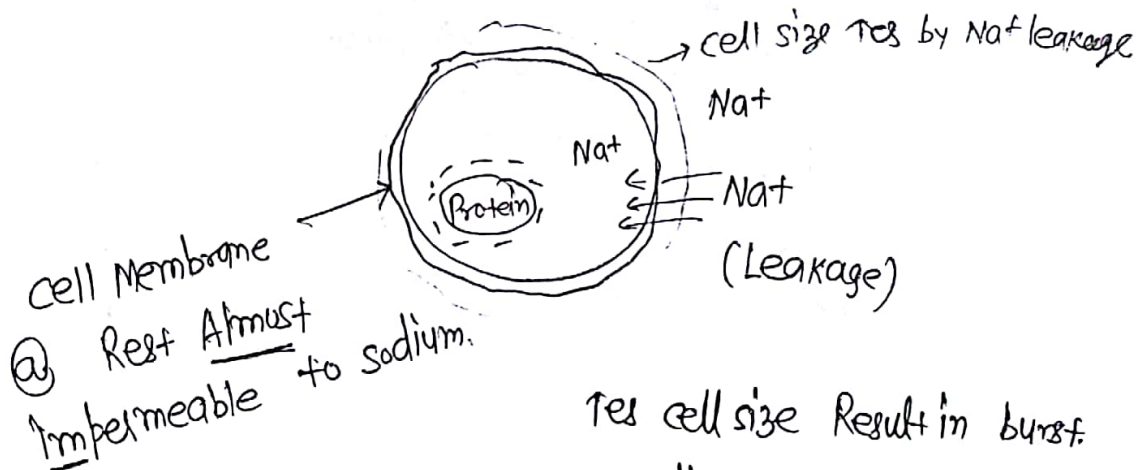
So, it contribute significantly to BMR

Q.Q.

Most imp. Function of $\text{Na}^+ - \text{K}^+ \text{ ATPase}$ Pump



Cell volume Regulation



res cell size Result in burst

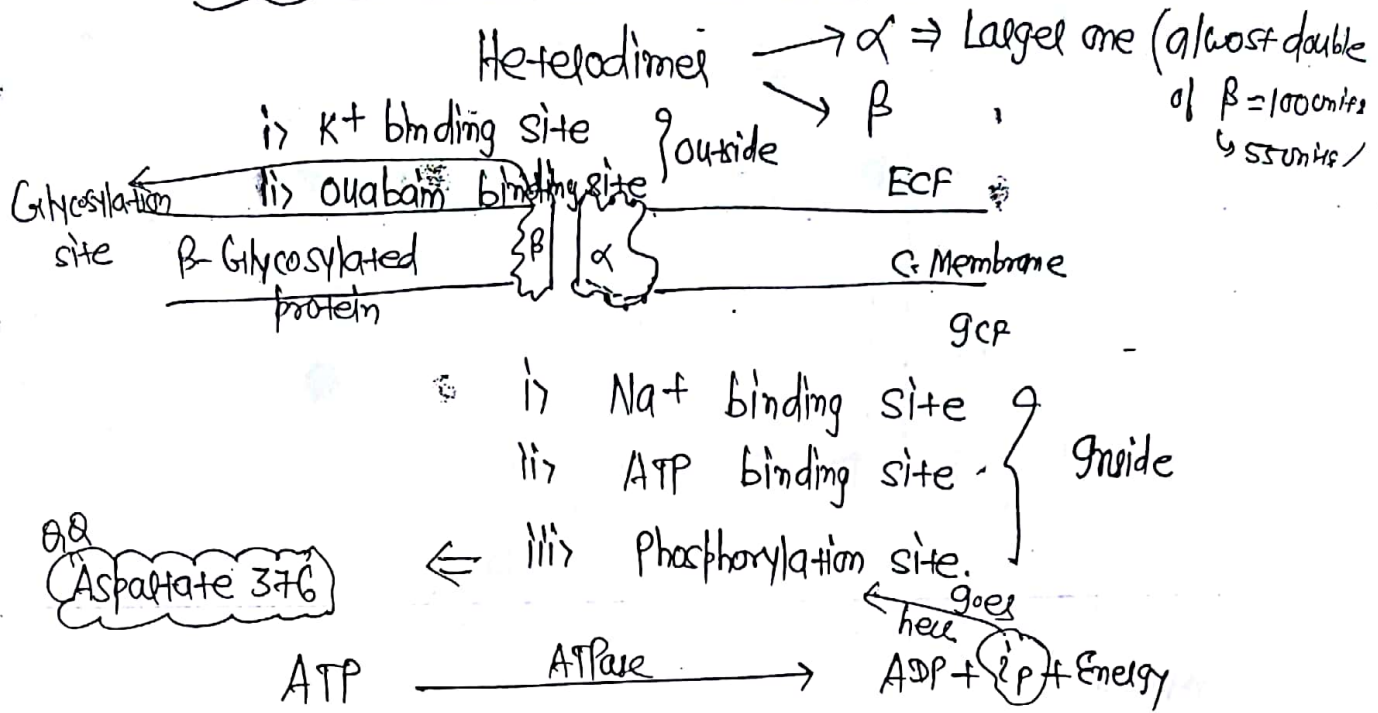


$\text{Na}^+ - \text{K}^+ \text{ Pump}$ do net loss of one osmotically active particle



Maintains cell volume

* Structure of $\text{Na}^+ - \text{K}^+$ ATPase Pump \Rightarrow

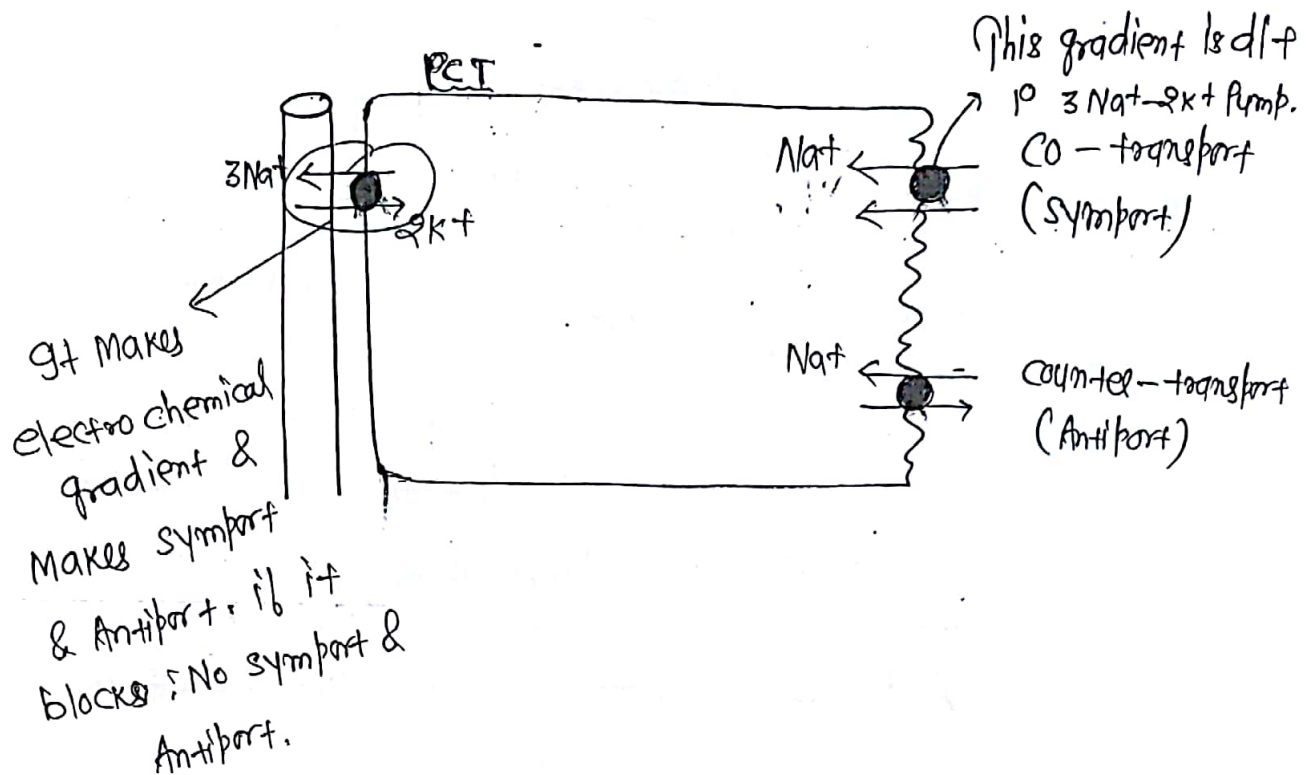


* All the binding site is prt. @ α -Unit.

• β -Unit has 3 extracellular Glycosylation sites.

* Hormones		<u>No. of $\text{Na}^+ - \text{K}^+$ ATPase Pump</u>	Activity $\text{Na}^+ - \text{K}^+$ ATPase Pump
① Thyroid	\rightarrow	Yes	\ominus
② Aldosterone	\rightarrow	\uparrow	\uparrow
③ Insulin	\rightarrow	\ominus	\uparrow
④ Dopamine	\rightarrow	\ominus	\downarrow
⑤ ANP	\rightarrow	\ominus	\downarrow

Secondary Active Transport



CO-transport in PCT \Rightarrow Na⁺ - Glucose
Na⁺ - Amino acid
Na⁺ - IP (Inorganic Phosphate)

CO-transport in Thick ascending Limb (TAL) \Rightarrow Na⁺ - K⁺ - 2Cl⁻ CO-transport

In DCT \Rightarrow Na⁺ - Cl⁻ CO-transport

In Intestinal epithelium \Rightarrow Na⁺ - Glucose CO-transport
Na⁺ - Amino Acid CO-transport

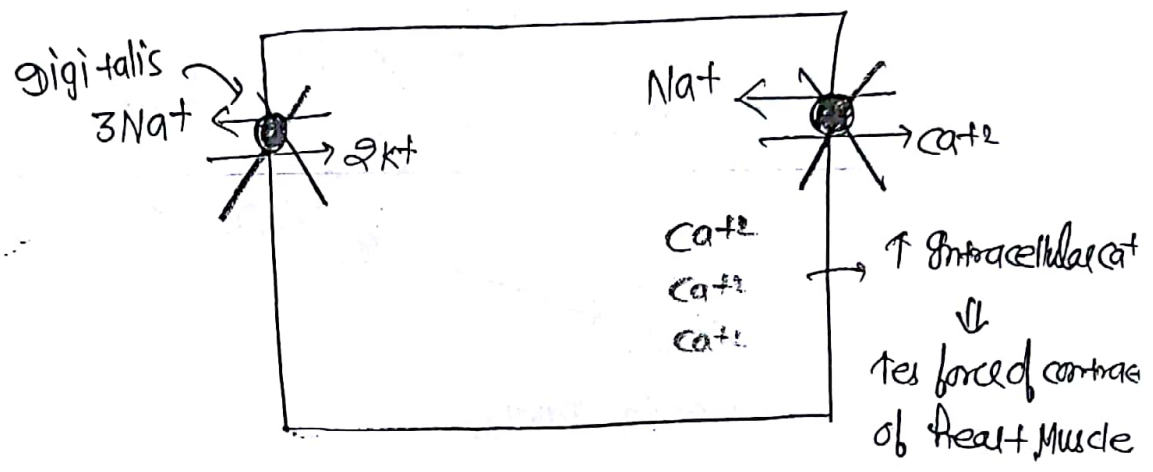
In distal ileum \Rightarrow Na⁺ - Bile salt CO-transport

In Thyroid \Rightarrow NIS (Na⁺ - Iodide Symport)

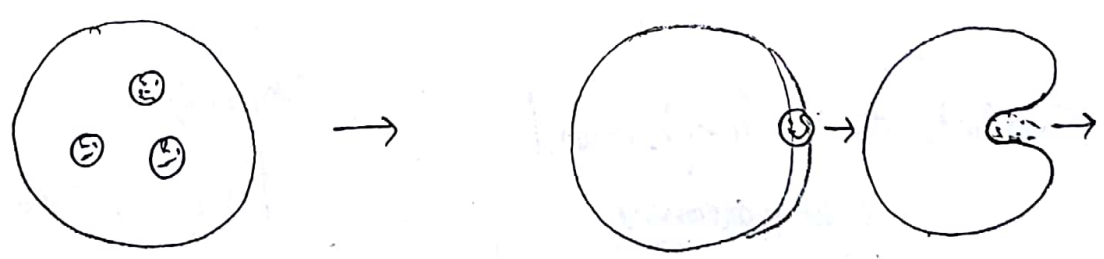
COUNTER TRANSPORT →

In PCT → $\text{Na}^+ - \text{H}^+$

In Myocardial cell → $\text{Na}^+ - \text{Ca}^{+2}$

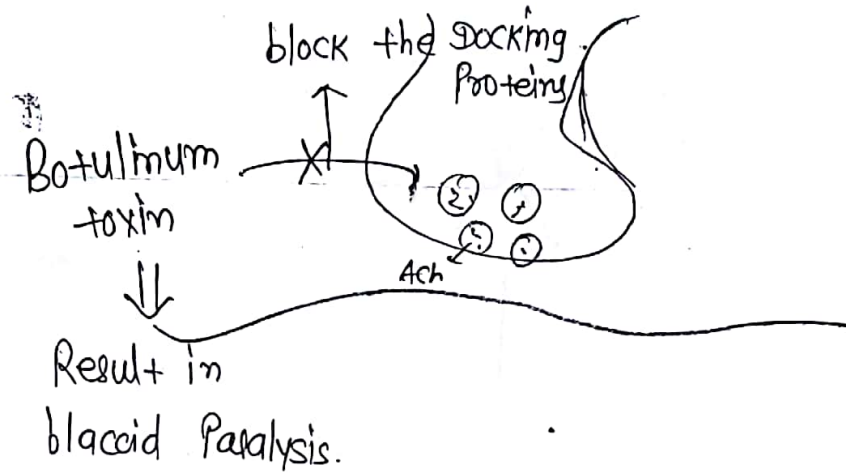
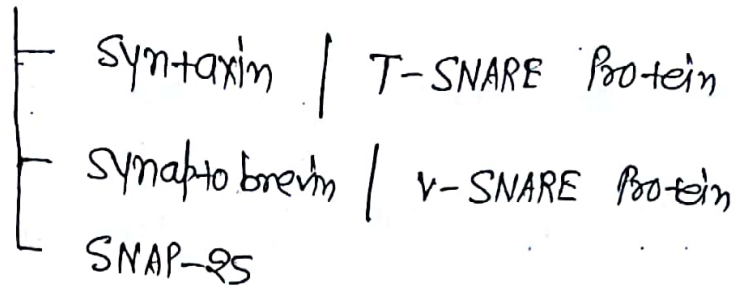


EXOCYTOSIS



- ↑ Total Area of cell Membrane
- We Need ⇒ Ca^{+2}
ATP
Docking Proteins

- Docking Proteins



- 2 Pathways of Exocytosis

Non-constitutive
OR
Regulated Pathway

Constitutive Pathway.

↳ also Regulated Pathway

↓
Synthesis of Enzyme/hormone/
Neurotransmitter

↓
Synthesis

↓ b/b; No storage
Release

↓ b/b
Processing

↓ b/b
Storage → Release

Min. imb. Steb

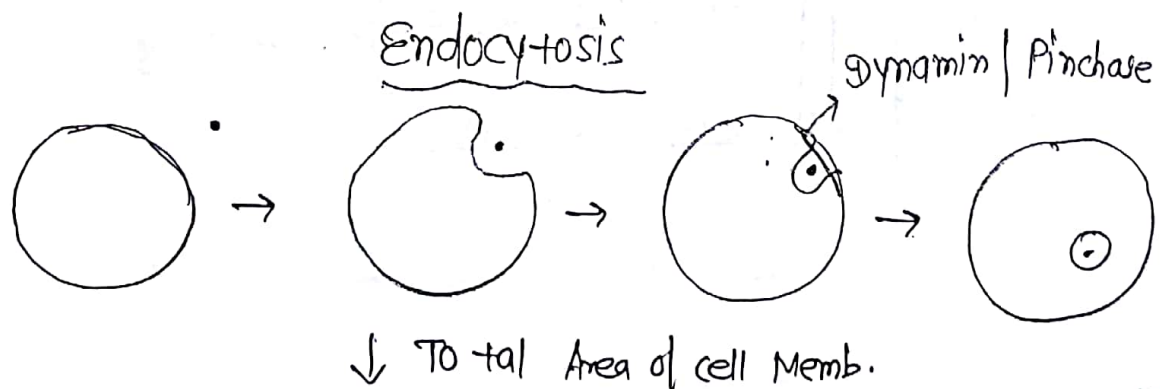
eg of Non-constituted Pathway \rightarrow

(17)

- Secretion of Insulin by β -cells
- Secretion of Glucagon by α -cells
- Secretion of ACh at NMJ;
- Secretion of serotonin by Raphe Magnus Nucleus cells
- Secretion of Enzyme by Pancreatic Acinar cells.

eg of constituted Pathway \rightarrow

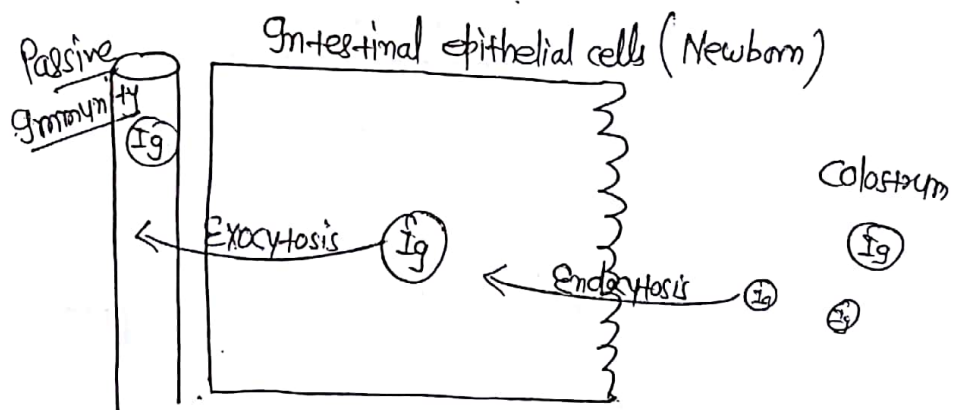
- Immunoglobulin by plasma cells
- Collagen by fibroblasts



\Rightarrow Endocytosis & Exocytosis occur simultaneously; Net area so; cell Membrane size = constant.

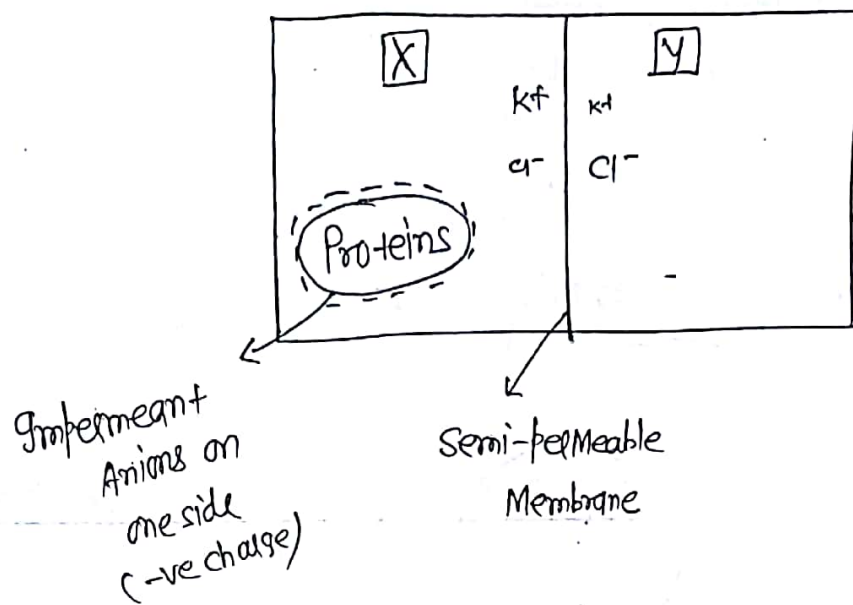
- Ca^{+2}
- ATP
- clathrin - Receptor Mediated Endocytosis
- caveolin - \oplus In Endothelial cells
 - For Absorption of Nutrients
- Dynamin/ Pinchase

TRANSCYTOSIS / CYTOPEMPSIS



(18)

DONNAN EFFECT \Rightarrow Seen on dissolvable ion
 \downarrow
 Cl^- & K^+



At eqm \Rightarrow $[K^+] \text{ in } X > [K^+] \text{ in } Y$
 $Cl^- \text{ in } Y > Cl^- \text{ in } X$

Result \Rightarrow i) Unequal distribution of dissolvable ion @ eqm;

ii) More No. of osmotically active particles on one side

Where to see \Rightarrow b/w Intracellular & Extracellular compartment
 - seen b/w Intravascular & Extravascular compartment

Gibbs - Donnan eqm \Rightarrow At eqm

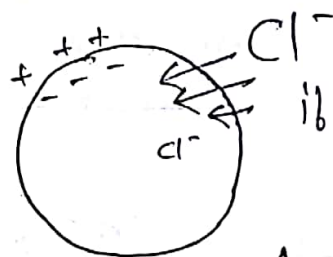
$$\frac{[K^+]_X}{[K^+]_Y} = \frac{[Cl^-]_Y}{[Cl^-]_X}$$

$$\Rightarrow \frac{[K^+_x] [Cl^-_x]}{[K^+_y] [Cl^-_y]}$$

Products of diffusible
ion on one side

Products of diffusible
ion on other side

* NERNST Equation \Rightarrow



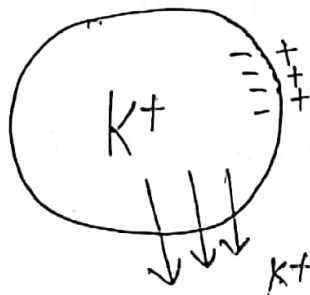
if cell memb. is free permeable to chloride



At a time \ominus ve charges inside the
cell repels Cl^- & stop movement



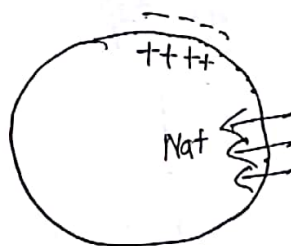
eqm potential (\ominus ve)



At a time \ominus ve charges inside (made
by K^+) cell attracts K^+ & stop movement



eqm potential (\ominus ve)



Na^+

At a time \ominus ve charges inside
cell repel Na^+ & stop movement



eqm potential (\ominus ve)

• If the cell Membrane becomes freely permeable to ion 39



Magnitude of potential difference for that ion at eqm k/as "eqm potential" Nernst Potential". It can be calculated by Nernst eqn :-

(There is No change in concn of ion @ eqm).

$$E_{(mv)} = \frac{2.3}{FZ} RT \log \frac{C_1}{C_2}$$

R = Gas constant

T = Absolute Temp.

F = Faraday constant

Z = valency

At $37^\circ C$,

$$\frac{2.3}{F} RT = 61.5$$

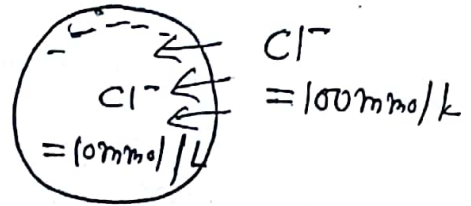
✖✖

$$E_{(mv)} = \frac{61.5}{Z} \log \frac{C_1}{C_2}$$

Q.Q.

$$2.3 \frac{RT}{F} = 60 \text{ mV}$$

$$E_{\text{Cl}^-} = ?$$



2 steps Method

i) calculate the potential

ii) Decide sign

$$E_{\text{Cl}^-} = \frac{2.3 RT}{FZ} \log \frac{C_1}{C_2}$$

$$= \frac{60}{1} \times \log \frac{100}{10} = \frac{60}{1} = 60$$

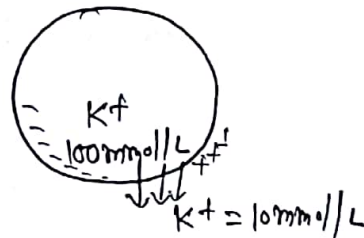
$$= \ominus 60 \text{ mV}$$

Q.Q.

$$2.3 \frac{RT}{F} = 60 \text{ mV}$$

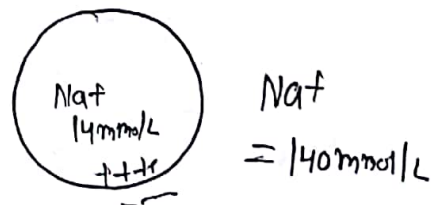
$$E_{\text{K}^+} = ?$$

$$E_{\text{K}^+} = -60 \text{ mV}$$



Q.Q.

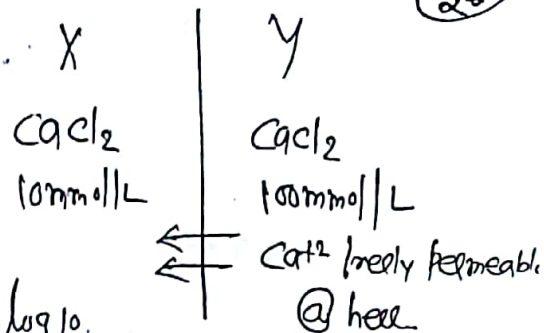
$$E_{\text{Na}^+} = +60 \text{ mV}$$



Q9 $\frac{2.3RT}{F} = 60 \text{ mV}$

$E_{Ca^{2+}}$ in X wrt to Y

$$\frac{2.3RT}{F \times 2} \log \frac{C_1}{C_2} \Rightarrow \frac{60}{2} \log 10 = +30 \text{ mV}$$



* (N) Value of E_{gm} potential \Rightarrow

$E_{K^+} = -90 \text{ mV}$
$E_{Cl^-} = -70 \text{ mV}$
$E_{Mg^{+2}} = 0 \text{ mV}$
$E_{Na^+} = +61 \text{ mV}$
$E_{Ca^{2+}} = +125 \text{ mV}$

Resting Membrane Potential

- GOLDMAN HODGKIN KATZ eqn OR constant field eqn
- Concn gradient of 3 ions (Na^+ , K^+ , Cl^-)
- cell Membrane permeability.

$$RMP = -61.5 \log \frac{C_{Cl^-} \times P_{Cl^-} + C_{K^+} \times P_{K^+} + C_{Na^+} \times P_{Na^+}}{C_{Cl^-} \times P_{Cl^-} + C_{K^+} \times P_{K^+} + C_{Na^+} \times P_{Na^+}}$$

A^+ Res^+ ; $P_{K^+} \gg \gg P_{Cl^-} > P_{Na^+}$

Q9

- Which ion contribute Max^m to RMP
- Most diffusable ion @ Res^+
- Cell Membrane is most permeable to which ion @ Res^+

K^+

Q9

Test Extracellular Na^+ ; effect on RMP??

a) More $\ominus ve$

b) Less $\ominus ve$

~~c) Same~~

*

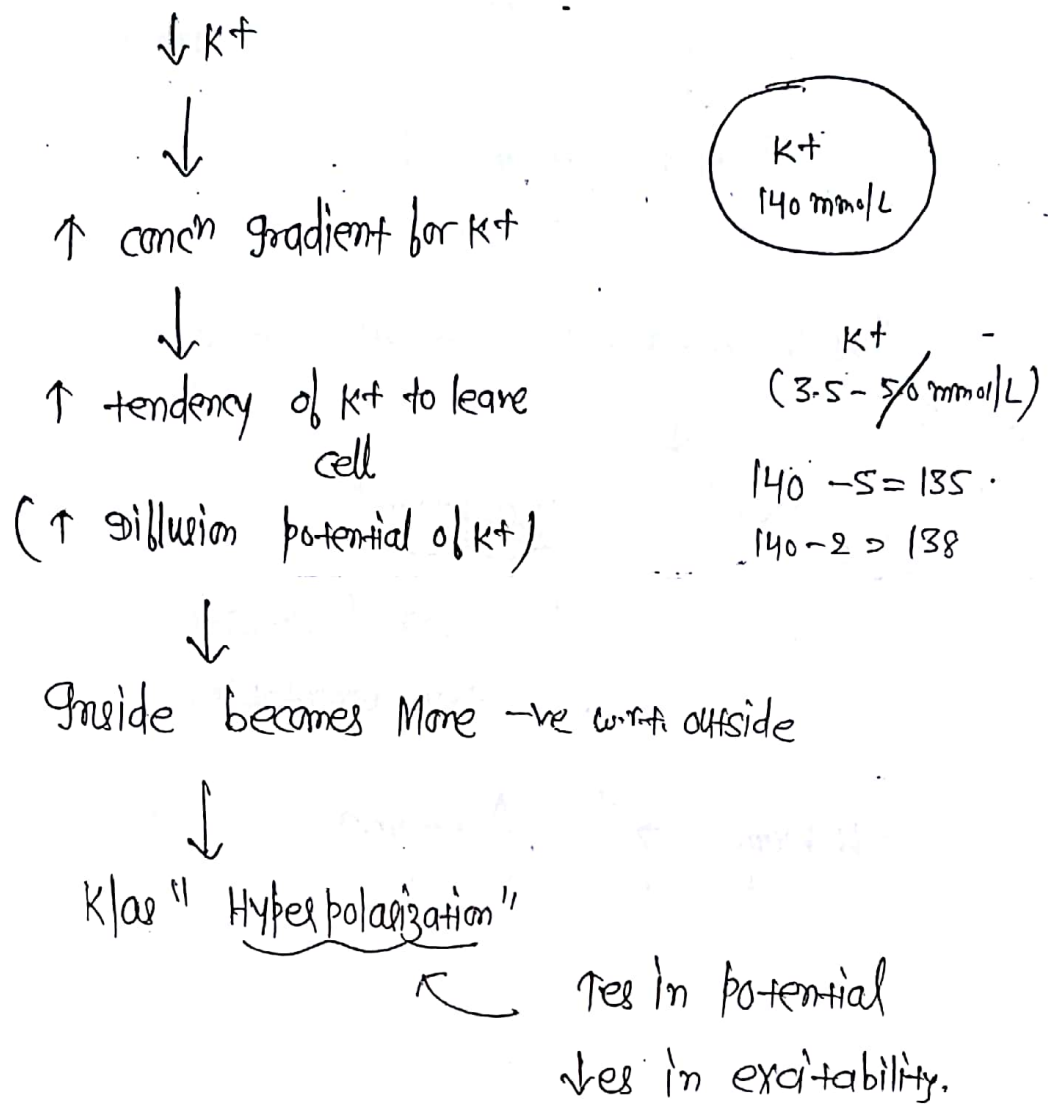
		<u>RMP</u>
Most Neurons	\Rightarrow	-70mv
Large Motor Neurons	\Rightarrow	-90mv
Skeletal Muscles	\Rightarrow	-90mv
Cardiac Muscles	\Rightarrow	-90mv
Pacemaker Cells	\Rightarrow	-50 to -60mv
Smooth Muscle cells	\Rightarrow	-45 to -65mv
Hair cells (cochlea)	\Rightarrow	-65mv
Rods & cones	\Rightarrow	-40mv
RBCs	\Rightarrow	-10mv

* RBC Membrane @ Res^+

$\hookrightarrow P_{Cl^-} > P_{K^+}$

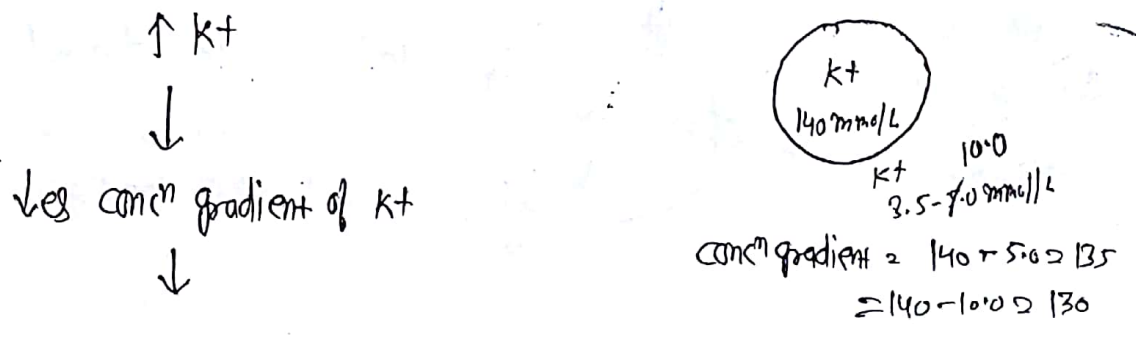
P_{Cl^-} = Permeability of Cl^-
 P_{K^+} = Permeability of K^+

Q.9. Effect of hypokalemia on RMP \Rightarrow



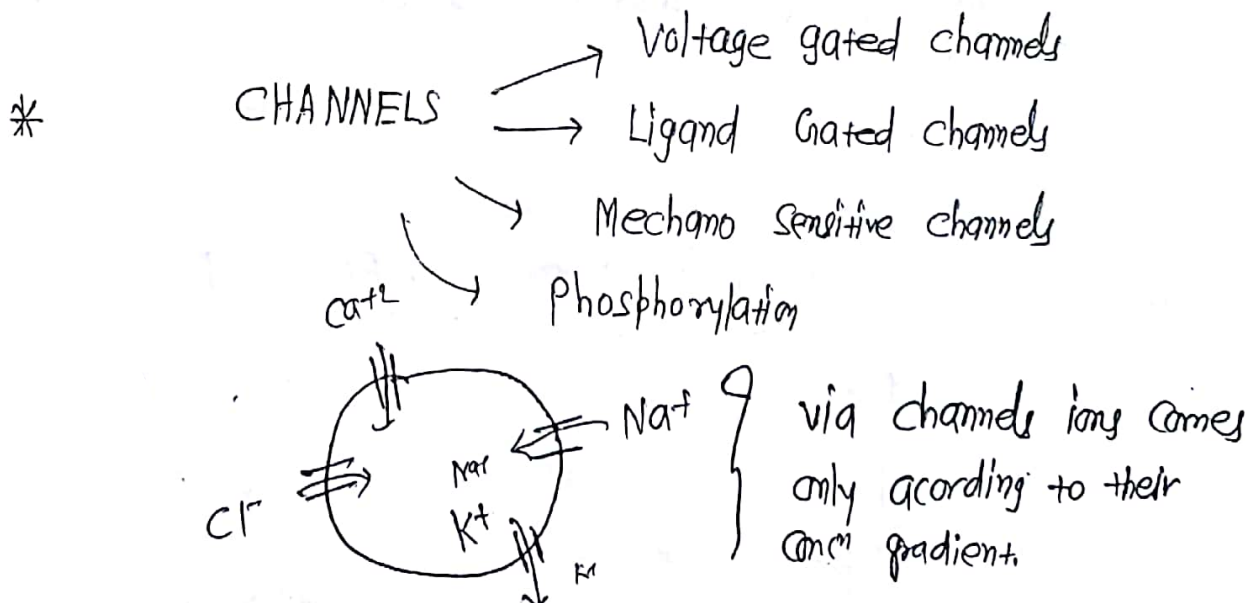
Symptoms \Rightarrow ① Muscle weakness (M/c symptom)

Q.10. Effect of hyperkalemia on RMP \Rightarrow



↓
 ↓ tendency of K^+ to leave the cell
 ↓
 ↓ diffusion potential of K^+
 ↓
 Inside becomes Less \ominus ve w.r.t. outside
 ↓
 K/a " Depolarization "
 ↳ ↓ Polarization
 ↑ excitability

M/c Symptom \Rightarrow Arrhythmia



• Dimer \rightarrow Cl^- channels (In bacteria, Animals) 22

• Trimer \rightarrow ENaC
 α, β, γ
 \swarrow
transport Na^+ .

• Tetramer \rightarrow K^+ channel



Aquaporin

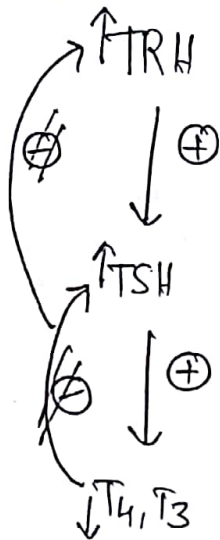


• Pentamer \rightarrow Cl^- channel (In humans)
Ligand gated channel (ACh Receptors)

FEEDBACK MECHANISM

Negative

- Most control system function as Negative feedback Mech^m.
- stabilizing Mech^m.



Positive

- eg \Rightarrow C = clotting;

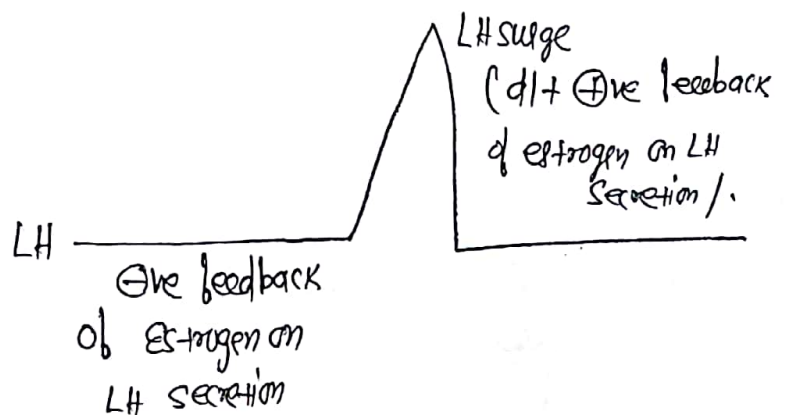
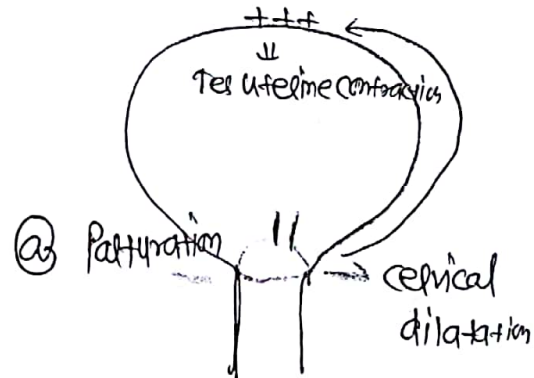
Ca^{2+} Release from Sarcoplasmic Reticulum during Muscle contraction.

L = LH Surge

A = Action Potential

P = Parturition

S = Shock

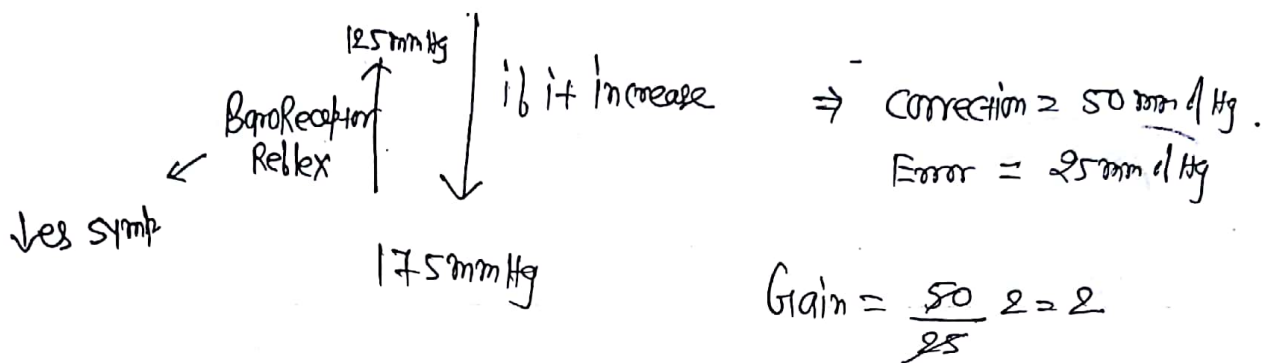


* Gain of the feedback system \Rightarrow

Gain \Rightarrow Correction over Error is gain, $= \frac{\text{Correction}}{\text{Error}}$

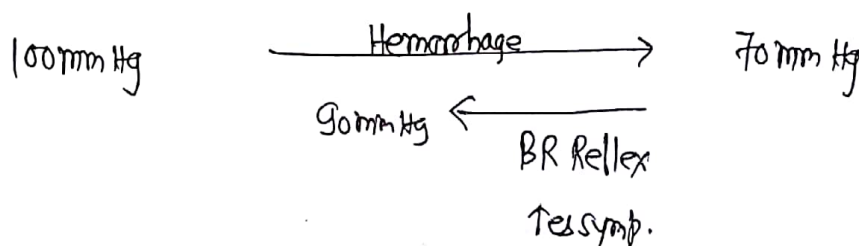
Q9

(N) Mean Arterial Pressure \Rightarrow 100 mm Hg



Q10

(N) MAP



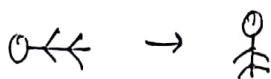
$$\text{Gain} = \frac{20}{10} = 2$$

*

Baroreceptor control Mechⁿ Temp. control system

Gain 2 ✓ (33) ✓

Q11



↓ In his BP by 10 mm of Hg;
Baroreceptor ↑ his B.P. by 8 mmHg

$$\text{Gain} \Rightarrow 4 = \frac{8}{2} = 4$$

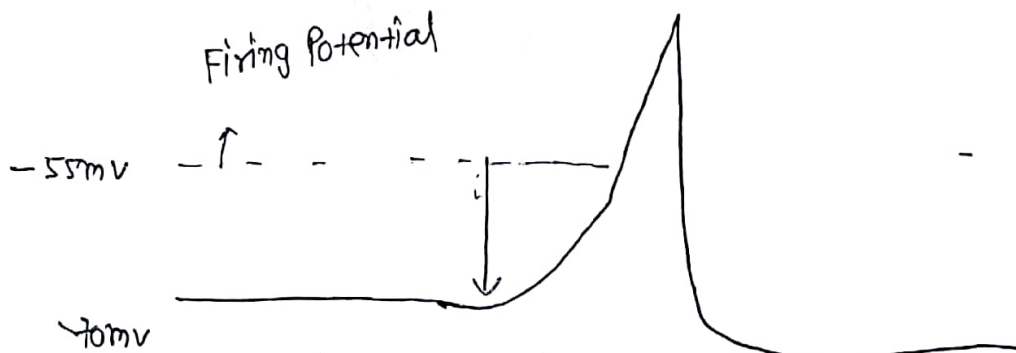
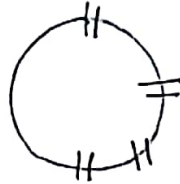
FEED FORWARD MECHANISM \Rightarrow k/a_s "Adaptive control"

↳ seen in control of Motor activity

29

NERVE PHYSIOLOGY

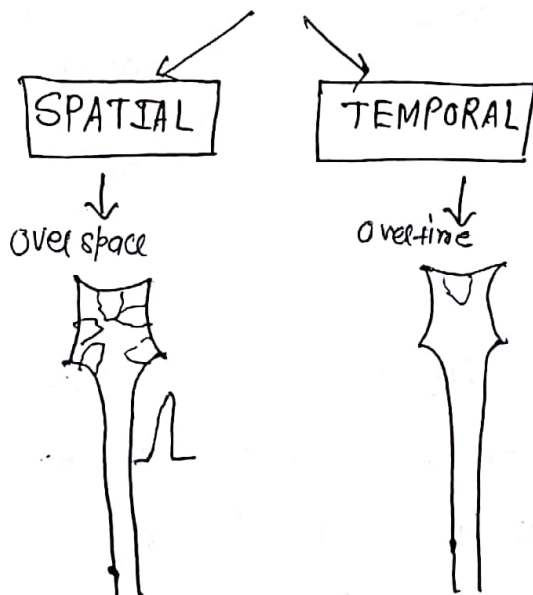
Local Potential & Action Potential ! →



Local potential

- Graded Response
- By Sub-threshold stimuli
- Decremental change
↳ dec over time & place.
- Not self propagated
- May/Mayn't followed by some action.

- Depolarising / Hyperpolarising
↓ ↓
EPSP IPSP (Inhibitory Post-synaptic Potential)
- Summation \oplus



No. of Sub-threshold
stimuli given simultaneously
↓
Produce Action potential

↑ frequency of
Sub-threshold
stimuli → produce
Action potential

Action potential (25)

- all-or-none Response
- by threshold or sub-threshold stimuli
- travel ~~not~~ decrement
- self propagated
- followed by some action
- Always depolarising.

- Summation \ominus

LOCAL POTENTIAL

eg \Rightarrow EPSP ;

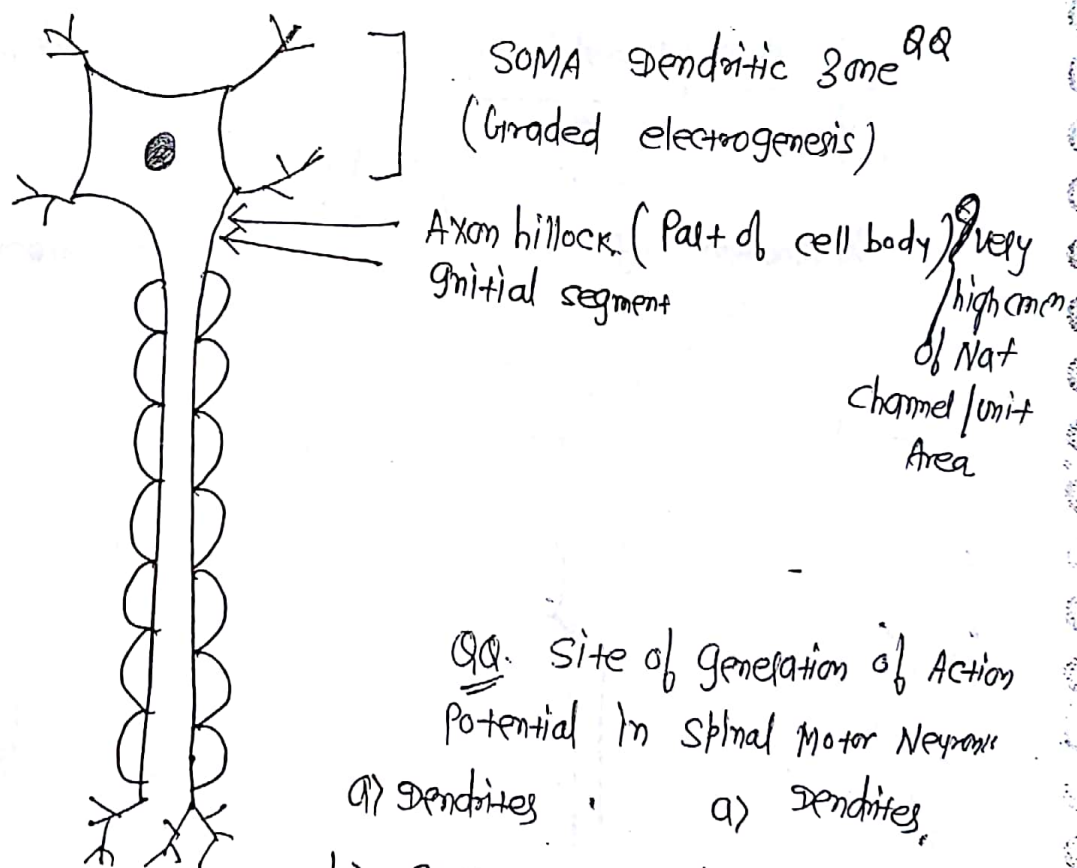
• IPSP ;

• Receptor potential ;
(Generator potential)

• Motor end plate potential
(A+ NMJ)

ACTION POTENTIAL

* Site of generation of Action potential \Rightarrow



Q. Site of generation of Action Potential in Spinal Motor Neuron

a) Dendrites

b) soma

c) Axon hillock

d) Axon

a) Dendrites

b) soma

c) A.H

d) Initial segment

* Initial segment can generate Action potential b/c (28)
 ↳ very high concn of Nat channel / unit area

Q9
 Concn of Nat channel / unit Area

Nodes of Ranvier \Rightarrow 2,000 - 12,000 / sq Micrometers

Initial segment \Rightarrow 500 $(\mu m)^2$

Surface of Myelin \Rightarrow 25 $(\mu m)^2$

↳
 Least

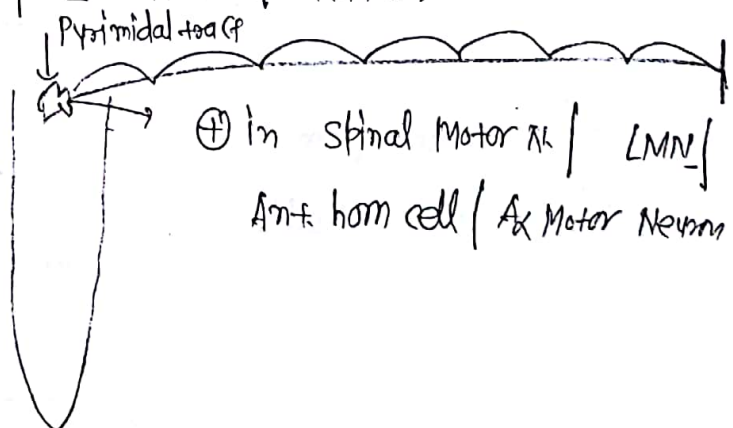
Q10
 Site of Generation of Action potential in Sensory Neuron!

i) Soma

ii) Dendrites

iii) Initial segments

↳ Initial / 1st Node of Ranvier



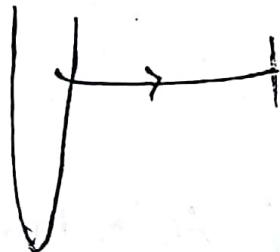
*

Spinal Motor Neuron

• Multipolar Neuron

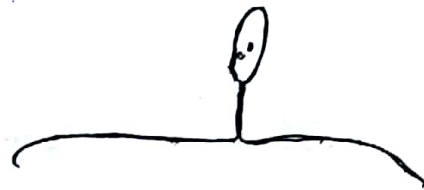


• Cell body - Ant. Horn of Spinal cord

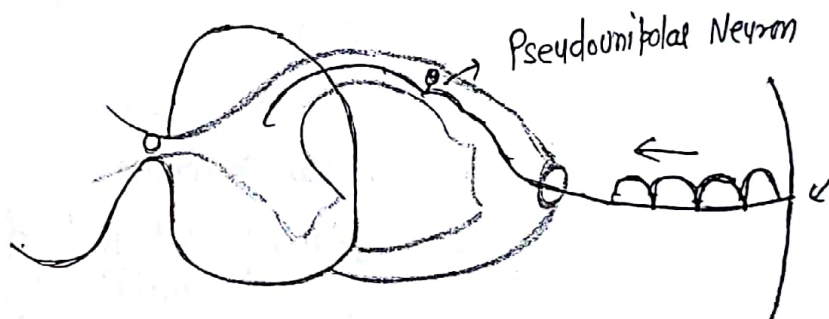
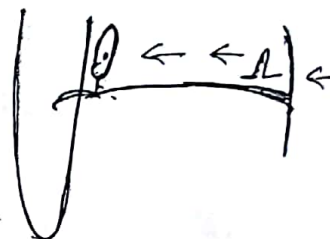


1st order sensory Neuron

• Pseudounipolar Neuron



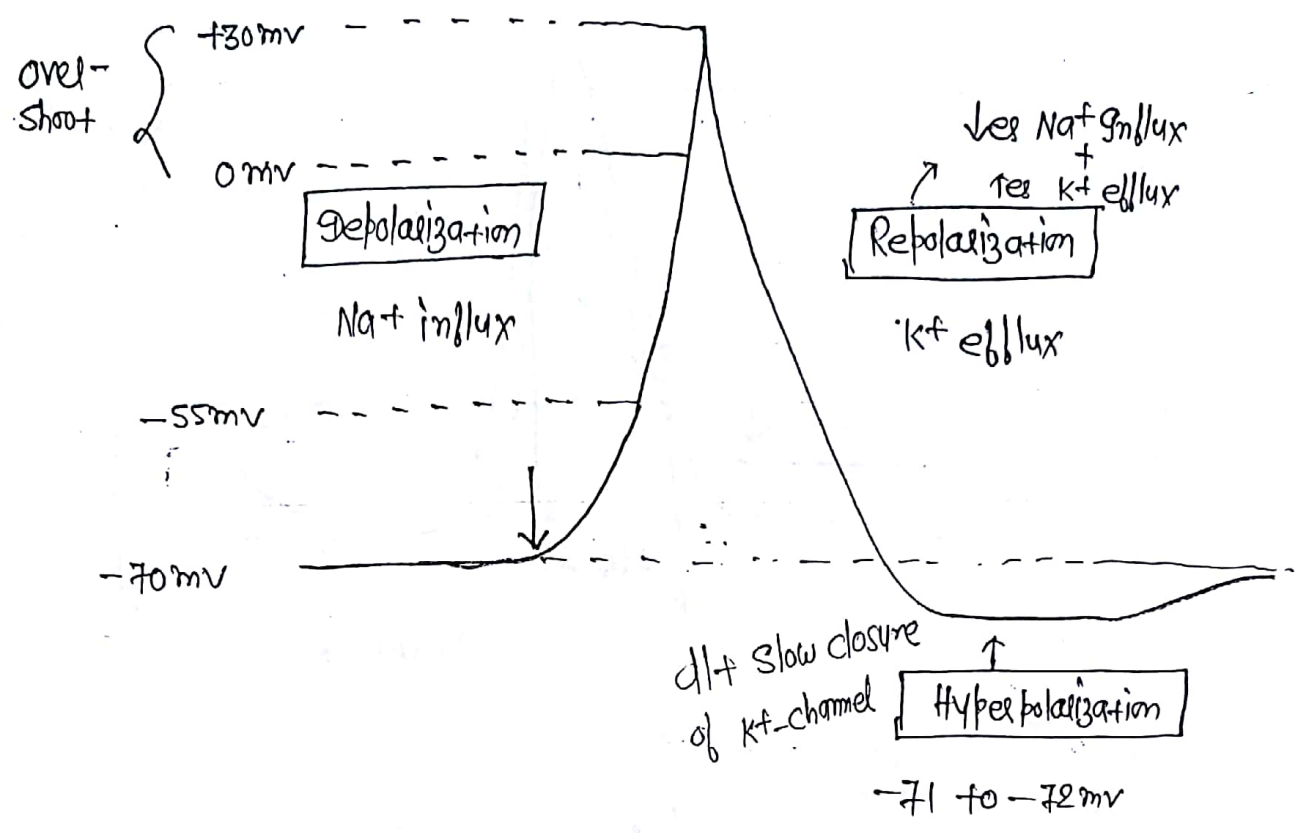
Dorsal Root Ganglion



• Carry impulses from Spinal cord to Periphery

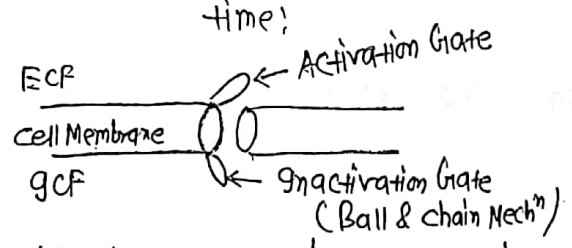
• Carry impulses from Periphery to spinal cord.

* Phases of Action potential \Rightarrow



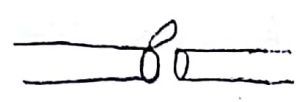
Na⁺ channels

- Fast channels
- -70 to +30mV
- closure is dependent on time

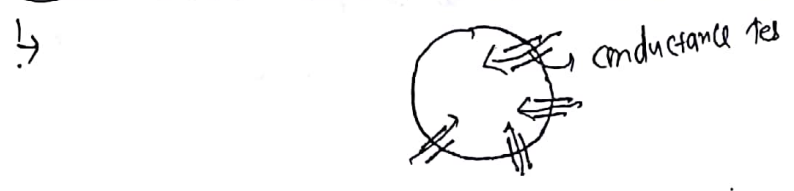


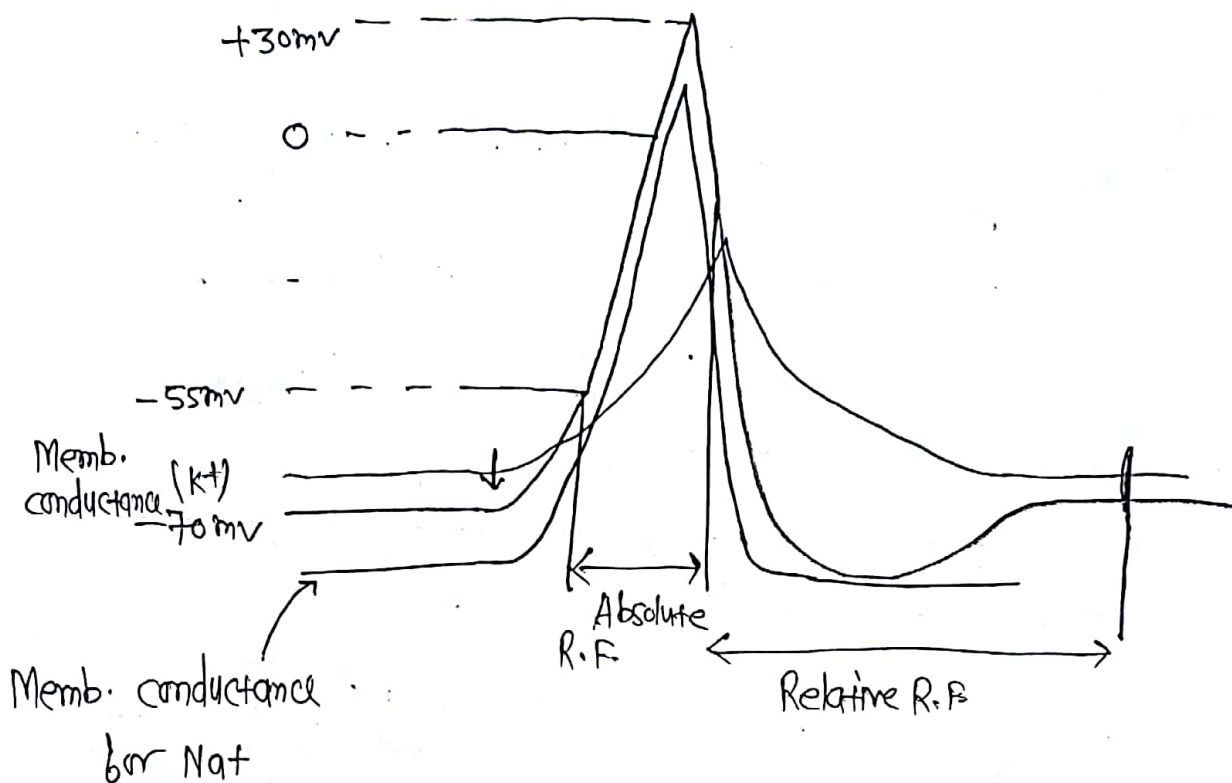
K⁺ channels

- Slow channels
- -70 to +30mV
- closure is dependent on time

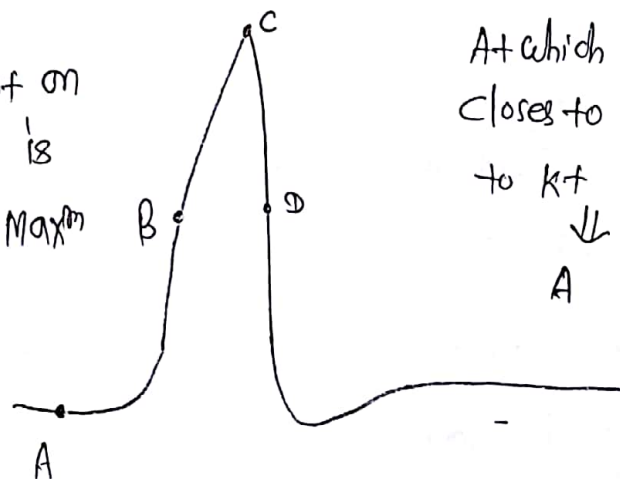


* Membrane conductance for Na⁺ & K⁺ during Action potential





Q. At which point on Action potential is Memb. conductance Max^m for Sodium
 ↓
 C



At which point on A.P. closes to equilibrium potential to K⁺
 ↓
 A

At which point Memb. conductance Max^m for K⁺
 ↓
 D

At which point on A.P. closer to E_{Na⁺} (eq^m potential of Na⁺)
 ↓
 C

REFRACTORY PERIOD

28

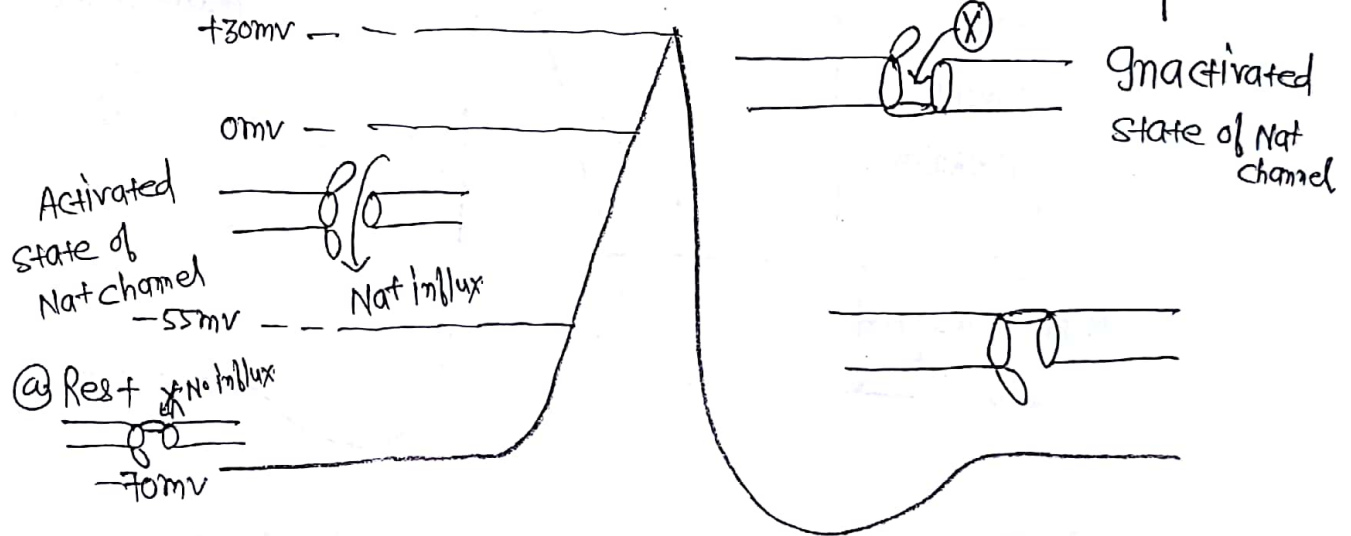
Absolute Refractory Period

From firing level
till Repolarization
is 1/3rd complete

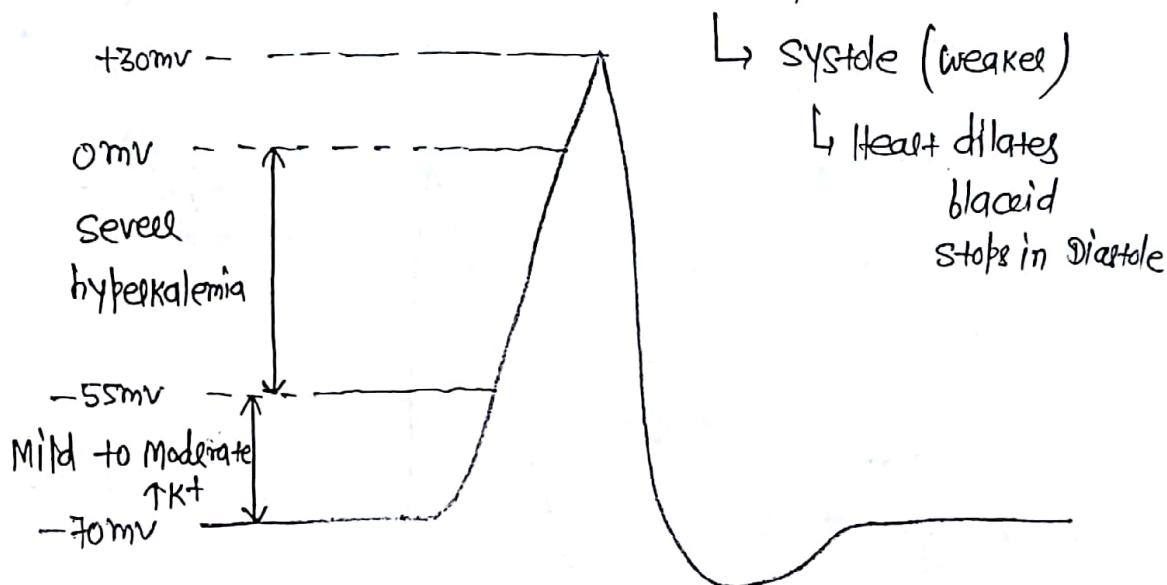
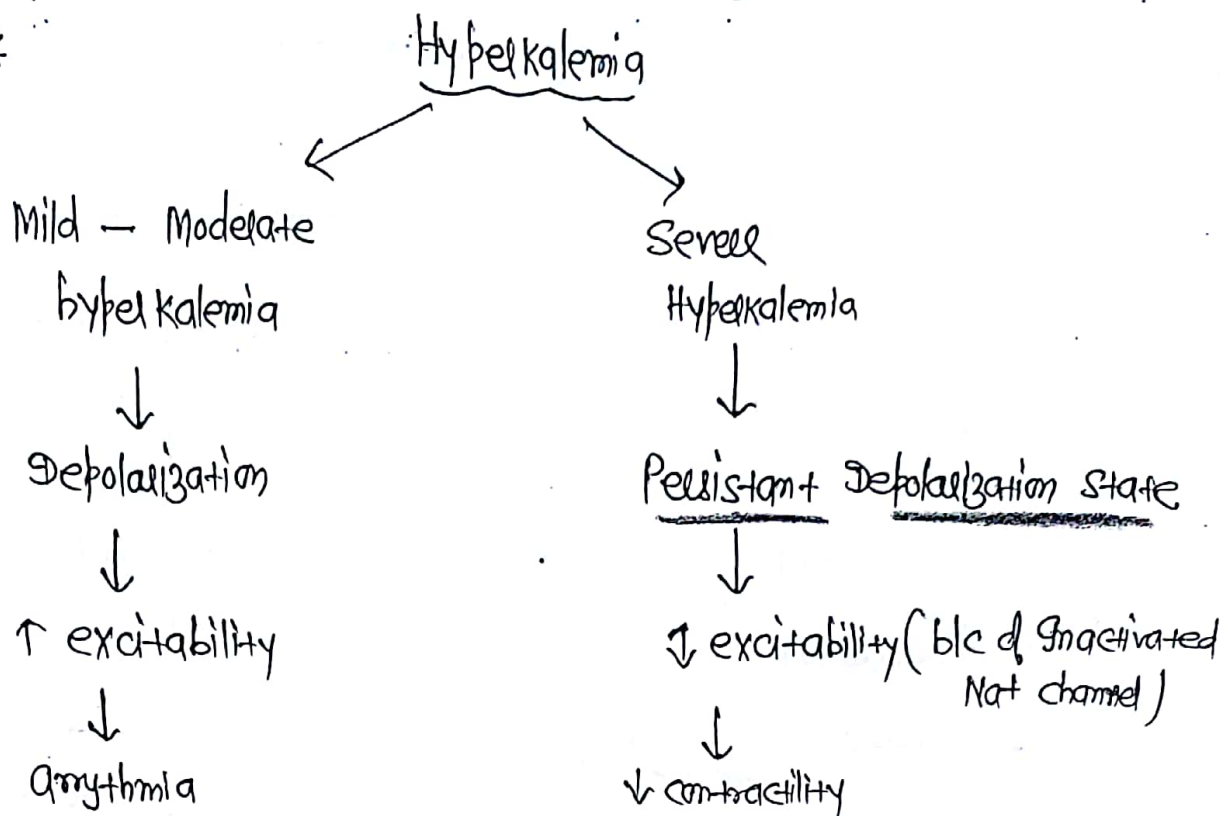
Relative Refractory Period

From 1/3rd Repolarization
till End of hyperpolarization

It is Responsible
for Absolute Refractory
Period



*



99.

Neuron is least excitable during →

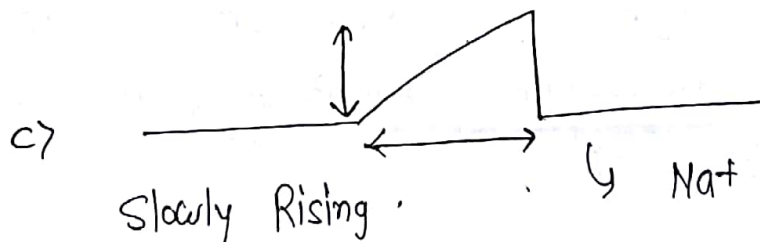
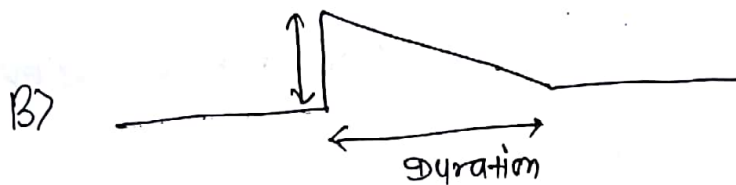
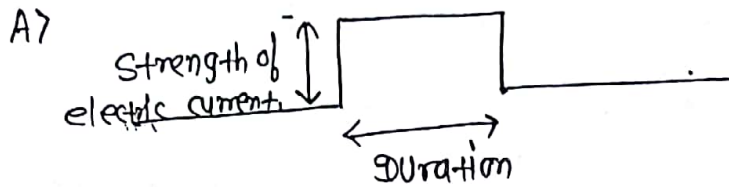
- a) Depolarization
- b) Repolarization
- c) Hyperpolarization

In hypercalcemia ⇒ Heart stops in systole
(calcium Rigor)

ACCOMMODATION

(29)

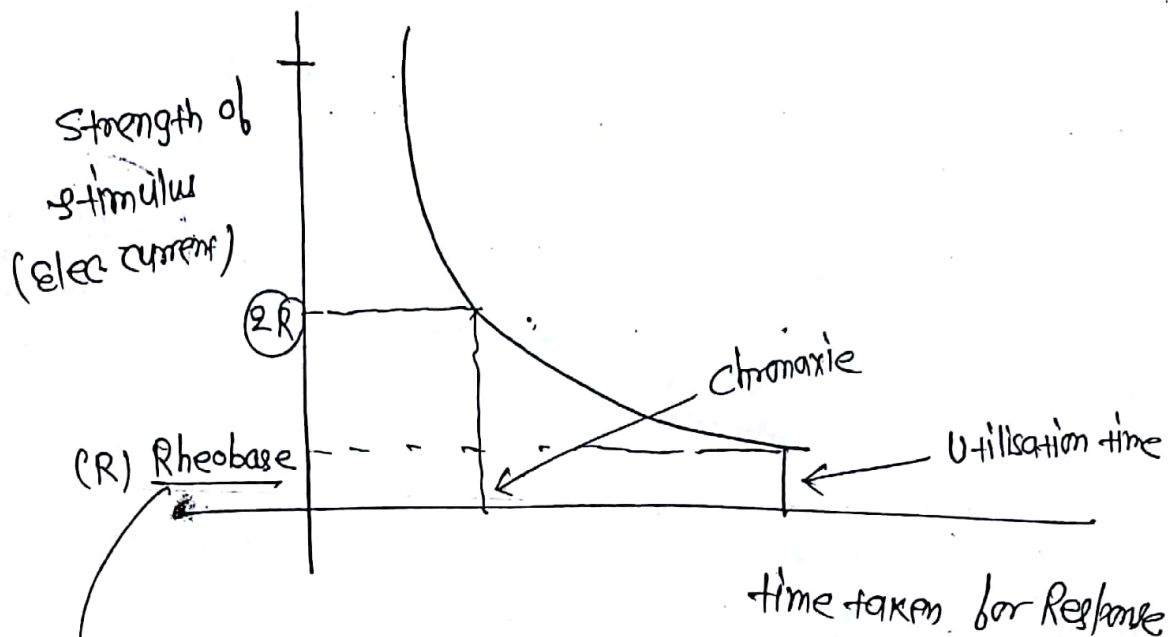
— It is slowly rising subthreshold stimulus; fails to produce a response. ↳ electric current.



Least Likely to Produce Response

↳ Na⁺ channel open & K⁺ also open
 ↳ b/c time taken to open; it has

STRENGTH - DURATION CURVE



Min^m strength of stimulus (E. current) \leq when applied for a prolonged / Not defined period of time; produces a Response

② Utilisation time \Rightarrow Time taken by Rheobase current to produce a Response.

Chronaxie \Rightarrow Time taken by a current which is twice the Rheobase

✱✱ { Lesser the Chronaxie \Rightarrow More excitable tissue }

Chronaxie (Nerve) < Chronaxie (SK, Muscle)

• Nerve fibres \Rightarrow
 $chr_A < chr_B < chr_C$

(A) (B) (C)
 \uparrow Diameter
 \uparrow Surface Area
 \uparrow No. of Na⁺ channel \downarrow time taken for Response

(30)

* $\text{Chromaxie}_{\text{Skeletal Muscle}} < \text{Chromaxie}_{\text{C.M.}} < \text{Chromaxie}_{\text{Smooth Muscle}}$

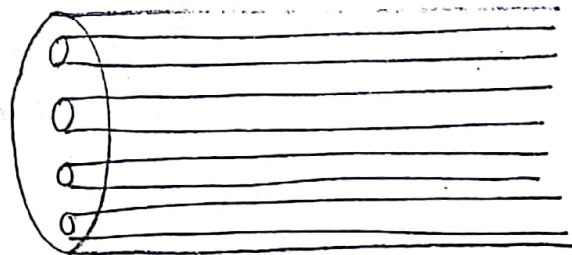
Q.Q. After N. Injury \Rightarrow Tes Chromaxie
but as Regeneration begins \Rightarrow Tes Chromaxie

* After N. Injury \rightarrow Strength-duration curve done in
Regular intervals

* FACTOR AFFECTING VELOCITY OF CONDUCTION OF
N. IMPULSE

① Diameter \Rightarrow Large diameter
 \Downarrow
 \uparrow Surface area
 \Downarrow
 \uparrow No. of Nat channel
 \Downarrow
Tes velocity.

$$\frac{1}{R} = \frac{1}{R_1} + \frac{1}{R_2} + \frac{1}{R_3} + \dots$$



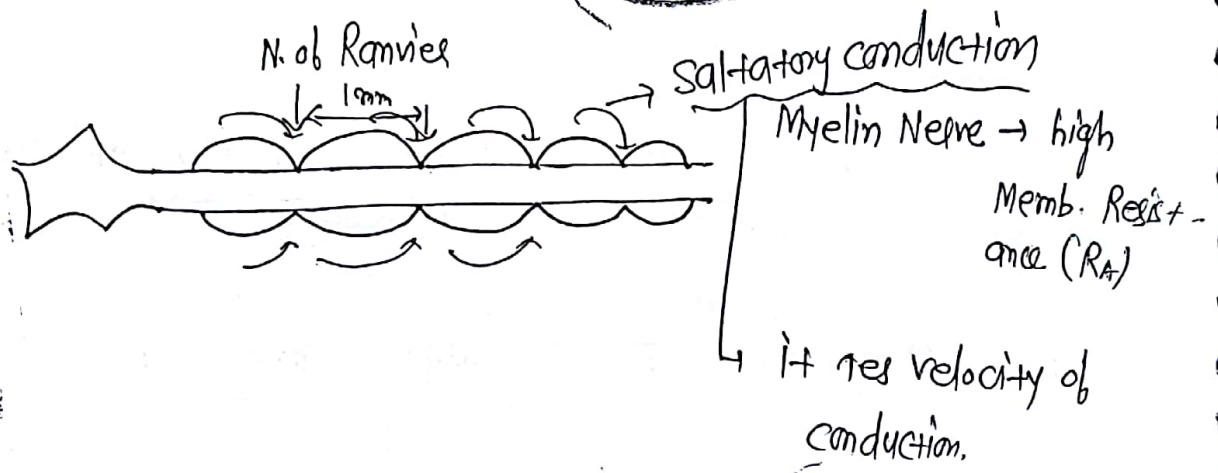
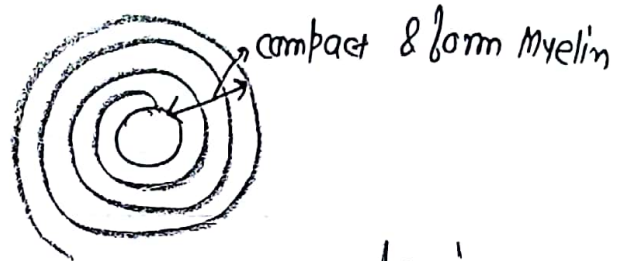
\uparrow Diameter \Rightarrow \downarrow Axoplasmic Resistance (R_A or R_m)
 \downarrow
 \uparrow Velocity of conduction

Q. Large diameter N. fiber has

- a) ~~Low R_A~~ ($\rightarrow \therefore$ res velocity)
b) High R_A

② Myelin \Rightarrow • Lipid Rich ;

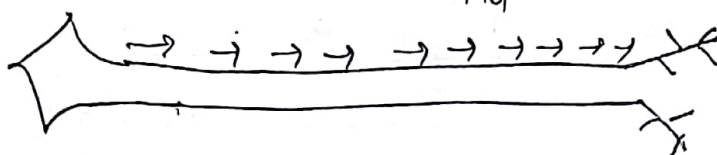
• Insulators. like
work



Q. A Large diameter ; Myelina N. fiber has
Low R_A ; high $\frac{R_m}{4}$ Membrane Resistance

Q. Fastest velocity \oplus in N. fiber has

High $\frac{R_m}{R_A}$ Ratio



Unmyelinated N. fibre

\Downarrow
Less Resistance, but
velocity Less as compare to
Myelinated N. fibre

* Small diameter always Unmyelinated.

33

③ Membrane capacitance \Rightarrow

cell Membrane \rightarrow High capacitance

\hookrightarrow Lipid bilayer

\hookrightarrow Acts as Parallel plate capacitor

+ Myelin



res Memb. Resistance

res Memb. capacitance

Q.Q.

Large diameter ; Myelin N. fiber has
Low R_A ; High R_m ; Low capacitance

Q.Q.

Fastest velocity \oplus in N. fiber \bar{c}
High Resistance Low capacitance
(R_m)

if Nothing in
question takes
 $R_m \Rightarrow$ Resistance

Q.Q.

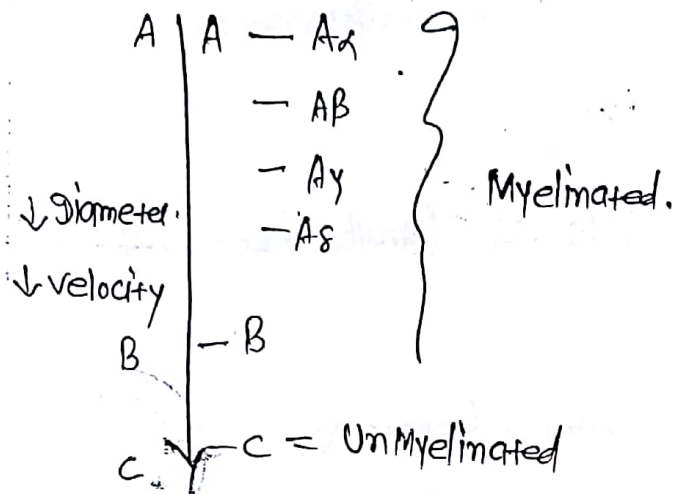
Nodes

\hookrightarrow Low Resistance ; High capacitance
(R_m)

CLASSIFICATION OF NERVE FIBERS

ERLANGER & GASSER CLASSIFICATION

- It is for Sensory, Motor; Autonomic kind of Neurons

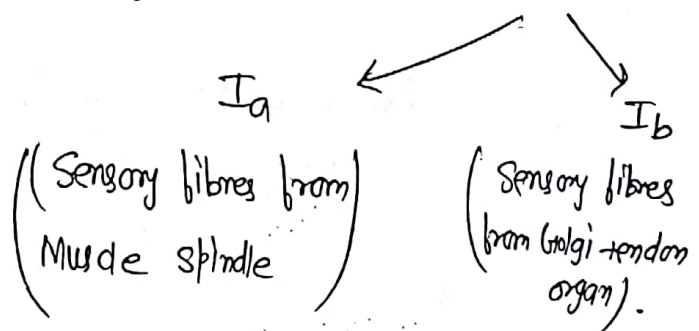


LYOD & HUNT'S CLASSIFICATION

- It is for sensory Neurons
- Numerical classification

A α = Somatic Motor —————> No Number given

Proprioception^(a) (Fastest Sensory conduction) —————> I



AB = Purely Sensory fibres

↳ for Fine touch; vibration

Proprioception (for Muscle spindle)

Deep pressure (PAIN)

II

A y = Motor fibres to Muscle spindle —————> No Number given

A_{δ} = Fast Pain, - Temperature (cold)
Somatic Mechanoreceptors

}

— III

(32)

B = Pine ganglionic Auto

— No Number given

C = Post ganglionic Sympathetic

— No Number given

→ Crude touch, Pressure, Slow pain,
Temp (cold & warmth); ITCH; Tickle

— IV

Total No. of Neurons = 100 Billion Neurons

↓

Glial cells >>> Neurons

- % of Human genes code for CNS = 40%

- Unmyelinated = Type IV

Afferent from Muscle spindle

- Most Myelinated = C

↓

- Fine touch = A_{β}

Ia, II

- Crude touch = C

Afferent from Golgi tendon organ

- Pressure = C

↓

- Deep pressure = A_{β}

Ib

- Vibration = A_{β}

Motor to Extramuscular Muscle fibers

- Slow pain = C

↓

- Fast Pain = A_{δ}

Ax

- Cold = A_{δ} & C

Motor to Intrafusal Muscle fibers

- Warm = C

↓

A_γ

SUSCEPTIBILITY

PRESSURE

$\Rightarrow A > B > C$

\swarrow
 A_{α} is More Susceptible (Saturday Night Palsy
 or Sunday Morning Palsy)

HYPOXIA

$\Rightarrow B > A > C$

LOCAL ANESTHESIA

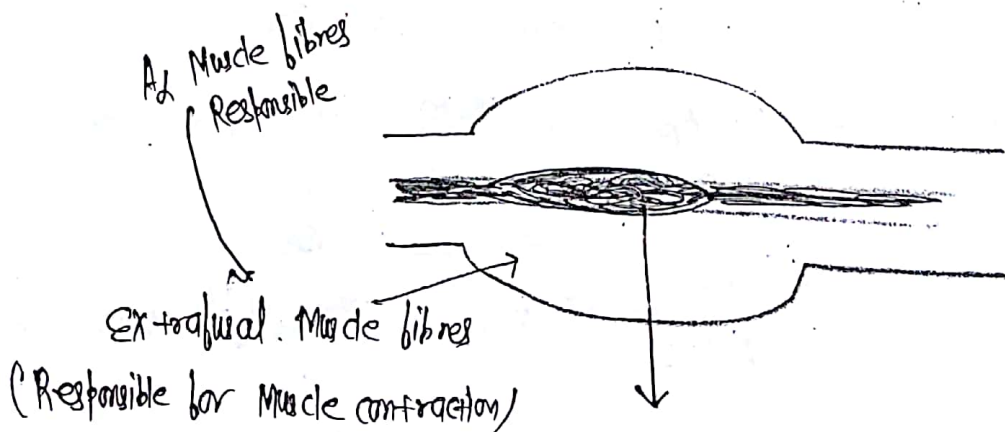
$\Rightarrow C > B > A$ X

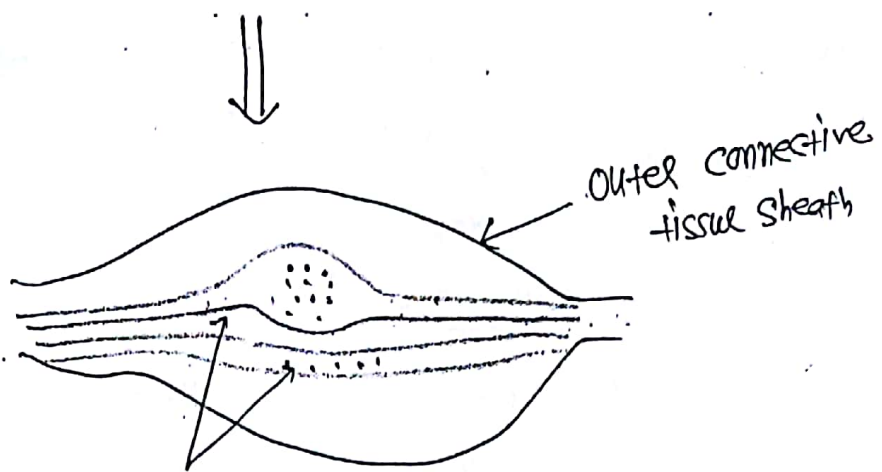
$B > C > A$ X

$A_{\gamma} > A_{\delta} = A_{\beta} > A_{\alpha} > B > C$ eg ALIMS Nov 18
 \downarrow Most Susceptible \downarrow Least Susceptible

MUSCLE SPINDLE

- Receptor for Muscle Length (Stretch)





Intrafusal Muscle fibres (5-6 in No.)

Nuclear Bag (1-3)

Nuclear chain (4-5 in No.)

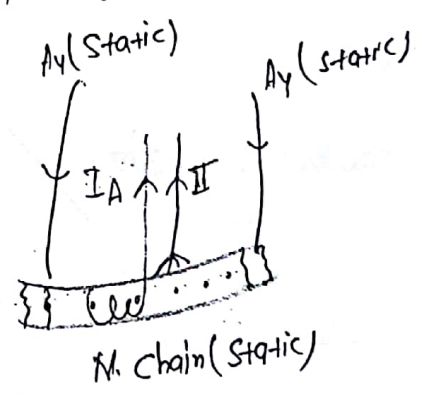
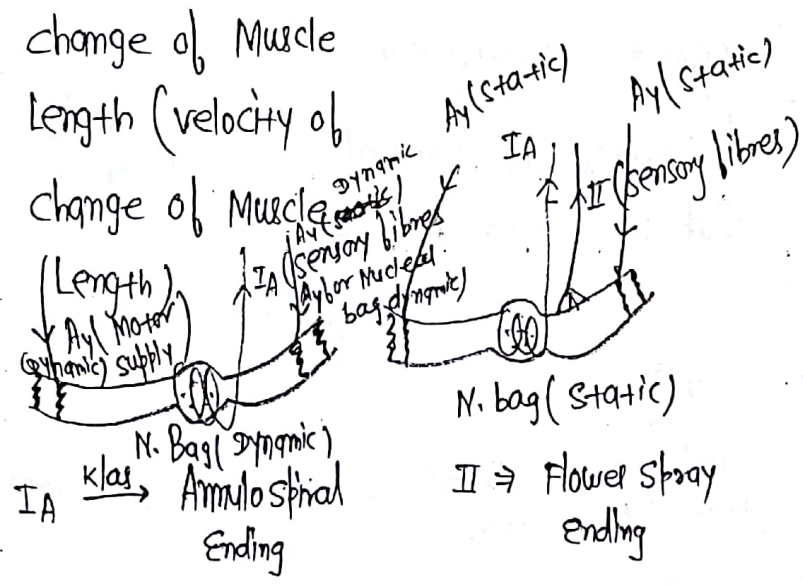
Nuclear Bag (dynamic)

Nuclear Bag (static)

Means for N. chain (Static Response)

Detects Rate of change of Muscle Length (velocity of change of Muscle Length)

Detect Steady Length.



* Muscle spindle can be stimulated in 2 ways \rightarrow

i) \uparrow Length of Muscle (Stretch)



Stimulate Muscle spindle

ii) \uparrow A γ Motor Neuron discharge



causes contraction of ends of Intrafusal Muscle fibers



stretches Receptor portion of Intrafusal Muscle fibers.



\uparrow Firing Rate

(Stimulate Muscle spindle).

AXOPLASMIC TRANSPORT

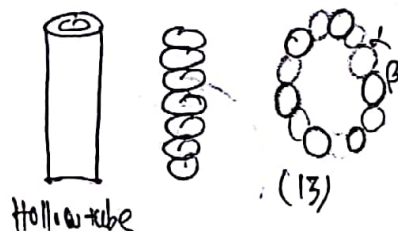
conduction of Action Potential



Ele.

\rightarrow Refers to Physical transport of Substance through Axoplasm

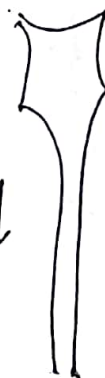
We Need Ca^{+2}

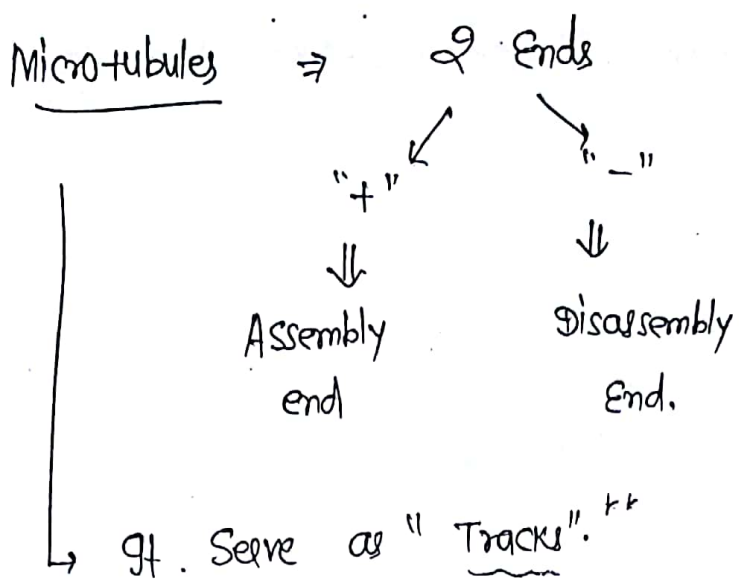


ATP
Microtubules
 \rightarrow Hollow tube
 \rightarrow Made of tubulins α β

Anterograde transport \downarrow

\uparrow Retrograde transport

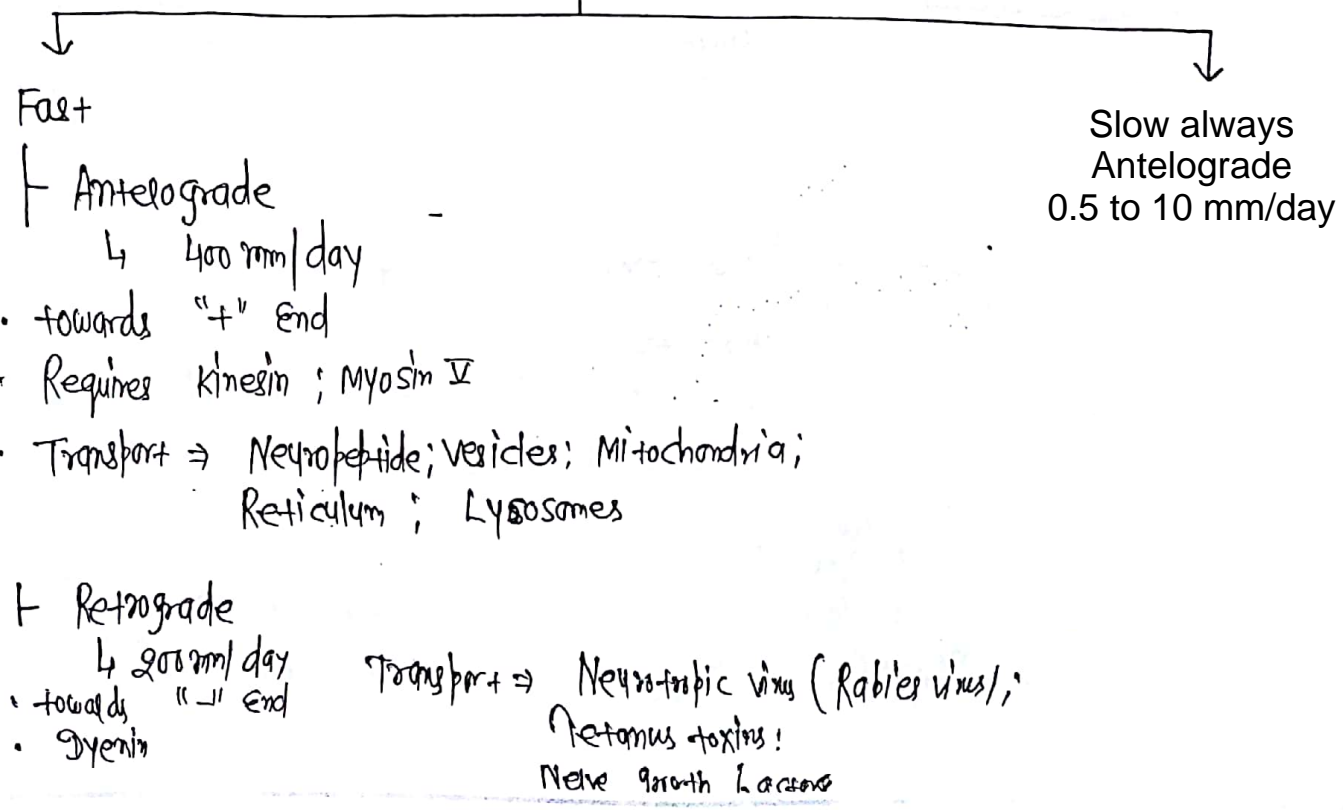




Microfilaments \Rightarrow Solid tubes
(Sometimes serve as "Tracks")

Molecular Motors \Rightarrow Kinesin
Dynein
Myosin V

Types of Axoplasmic transport



Q8 Neurofilaments doesn't Require for Axoplasmic transport

WALLERIAN DEGENERATION

• Seddon's classification of Nerve Injuries →

NEUROPRAXIA ⇒ Temporary loss
of function

Degeneration

Regeneration

AXONTEMESIS ⇒ Nerve is
Intact

+

+

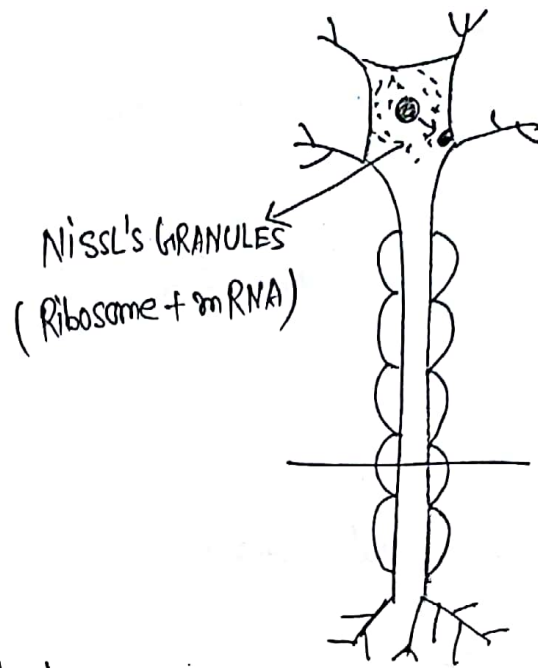
NEURONTEMESIS ⇒ Nerve is
destroyed

+

—

WALLERIAN DEGENERATION

35



Change in cell body

⇒ early 24-48 hrs

↳ Chromatolysis

Nucleus Moves to Periphery

Change in distal segment

Within few hours of injury

↳ Swelling of Axis cylinder

In 3-5 days

↳ Axonal degeneration

8th day

↳ Myelin Degeneration starts

32nd day

↳ Myelin Degeneration complete

* Similar changes in Proximal segment but upto Nearest Node of Ranvier

Q.8 1st change after N. injury ⇒

a) Chromatolysis

b) Axonal deg.

a) chromatolysis

b) Axonal degeneration starts (swelling)

Sequence of events after Axonal Injury ⇒
 Chromatolysis → Axonal degeneration

↓
 Ghost tube ← Myelin degeneration

Regeneration ⇒

Sprouting of Axonal stump

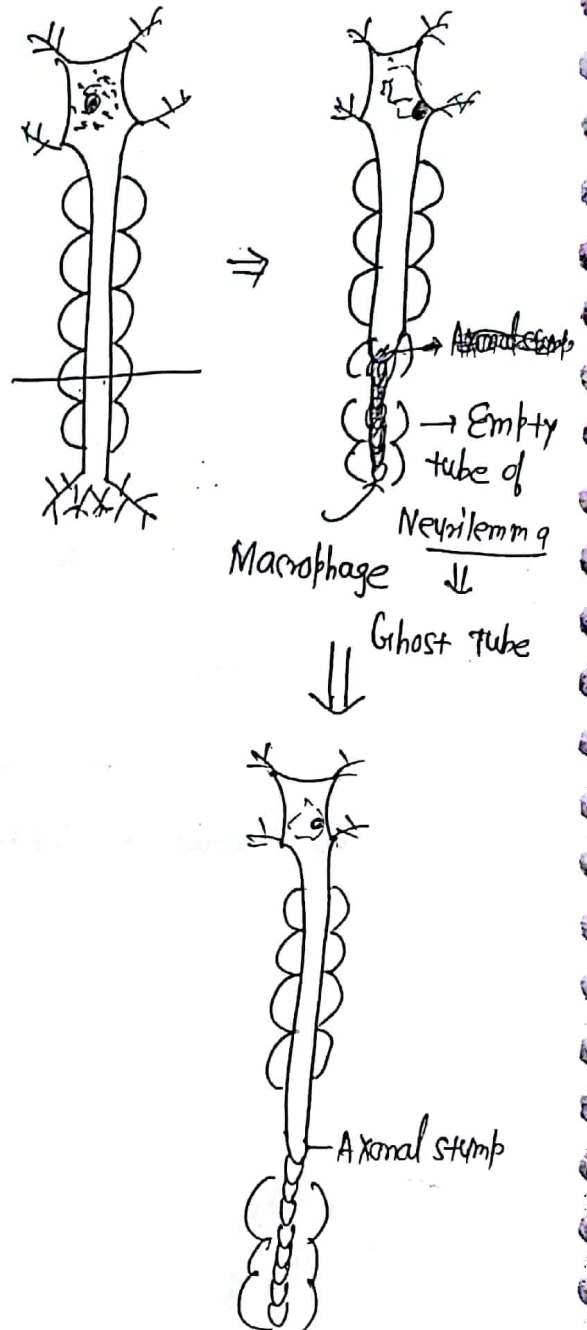
↓
 Enters into Ghost tube

↓
 Myelin is Laid down
 in sheets

• Rate of Regeneration

↓
 1mm/day or 1inch/Month.

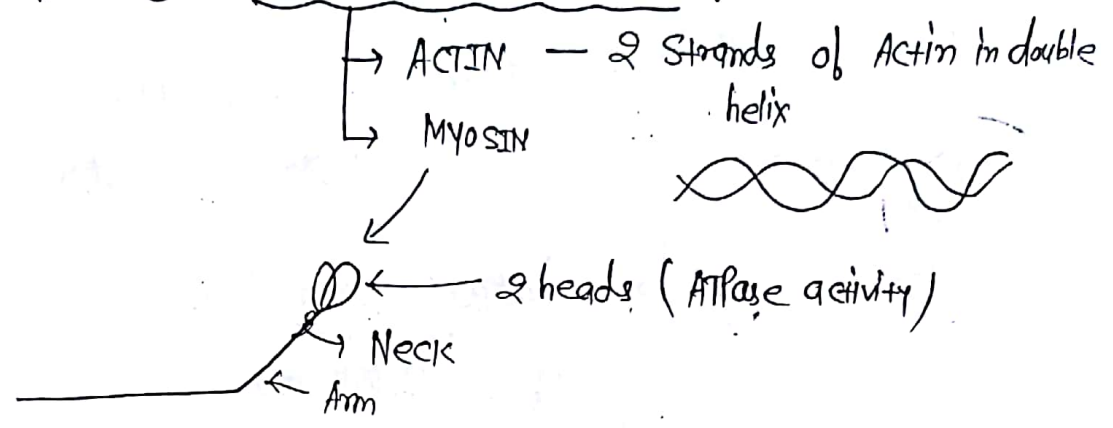
⇒ Regeneration usually complete by
 1 year



SKELETAL MUSCLE PHYSIOLOGY

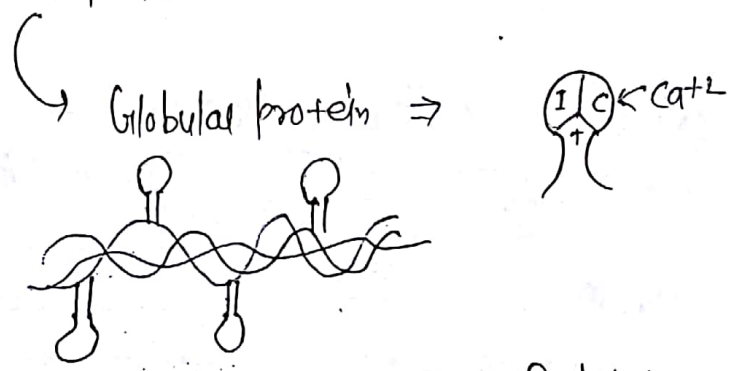
- Skeletal Muscle
 - Voluntary
 - Striated

They have \rightarrow ① CONTRACTILE PROTEINS \rightarrow



② Regulating proteins \rightarrow

- Tropomyosin \rightarrow 1 Molecules of Tropomyosin covers 7 Active Site of Actin
- Troponin



\downarrow after Ca^{+2} attaches to Troponin-c
Conformational change in Troponin

\downarrow
causes Tropomyosin to slide

\downarrow
Result in Active Site on Actin

\downarrow
Actin-Myosin cross bridge formation cross bridge cycling

③ Structural Protein \Rightarrow

\hookrightarrow Actinin \Rightarrow binds actin to Z-Line

Titin \Rightarrow binds Z-Line to M-Line

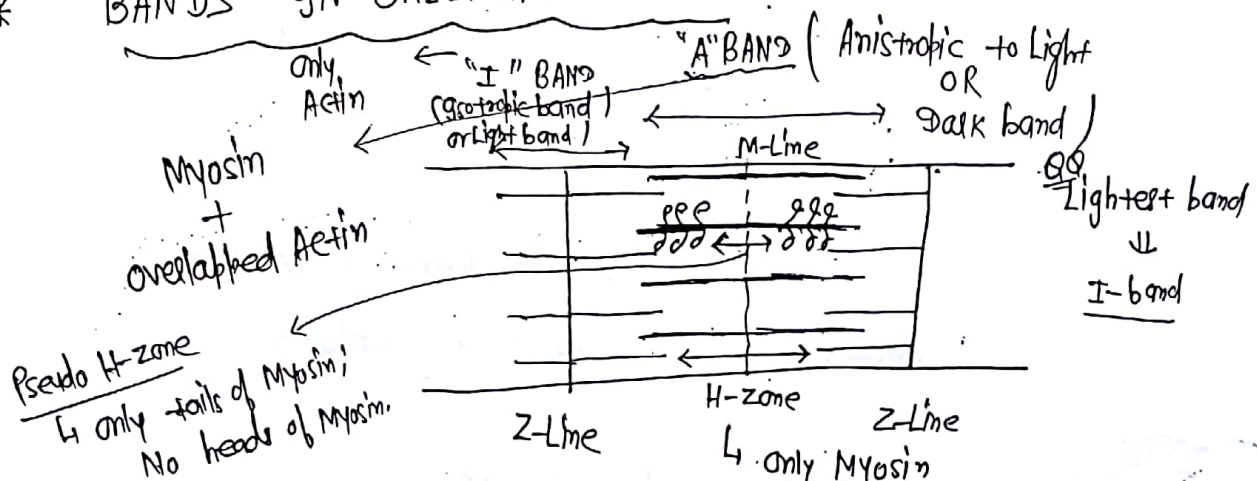
- \hookrightarrow Responsible for Elasticity
- \hookrightarrow Forms "Scaffolding"
(Structural Support)
- \hookrightarrow Largest known protein

$$M_w \approx 3,000,000$$

Mutation in Titin \Rightarrow Tibialis Muscular dystrophy

Desmin \Rightarrow Binds Z-Line to Plasma Membrane

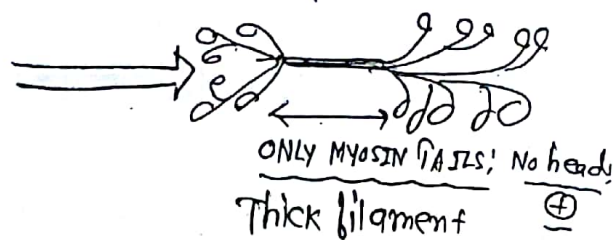
* BANDS IN SKELETAL MUSCLE \rightarrow



SARCOMERE $\Rightarrow \frac{1}{2} \text{ I-Band} + \text{A-band} + \frac{1}{2} \text{ A-band}$

M-Line \Rightarrow Connect Myosin molecules to each other

B/w two z-line = sarcomere.



"Bunch of Golf sticks"

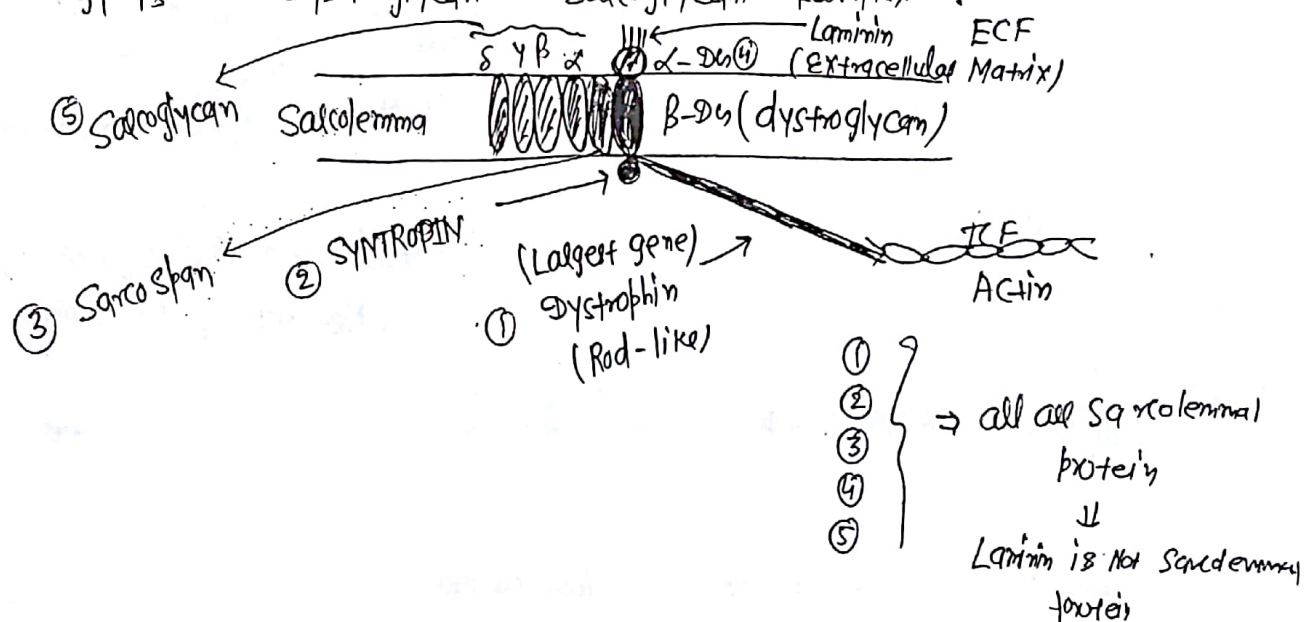
* Pseudo H-Zone \Rightarrow Formed by Reversal of Polarity of Myosin heads.

* During Muscle contraction \rightarrow The I-band \downarrow
H-zone = \downarrow | disappears
(QA) A-band = UNCHANGED

SARCOLEMMA PROTEINS

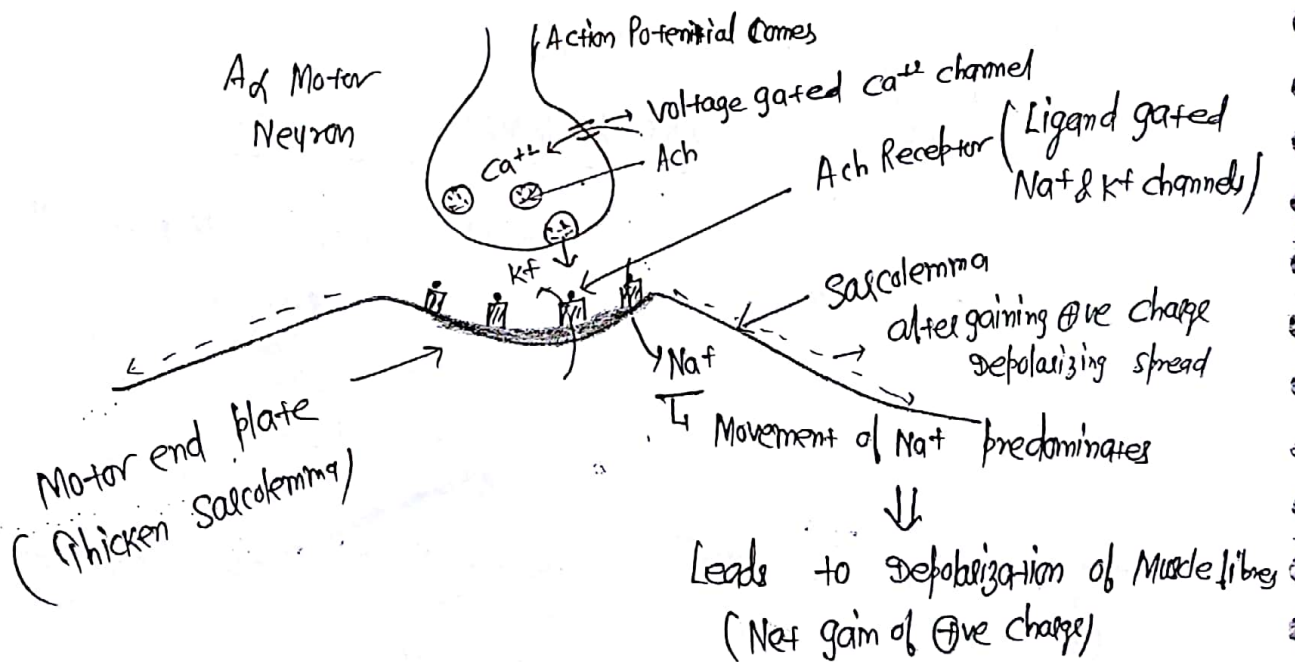
Muscle fiber = Muscle cell

* It is "Dysotroglycan - Sialotroglycan" Complex.



- if dystrophin $\ominus \Rightarrow$ Duchenne's Muscular dystrophy
- if dystrophin \oplus , but Reduced \Rightarrow Becker's Muscular dystrophy
- if Sarcoglycan Mutation \Rightarrow Limb Girdle dystrophy
(Mutation of sarcoglycan)
- * Function of dystrophin \Rightarrow Probably Amplifies force generated
by Actin & Myosin.

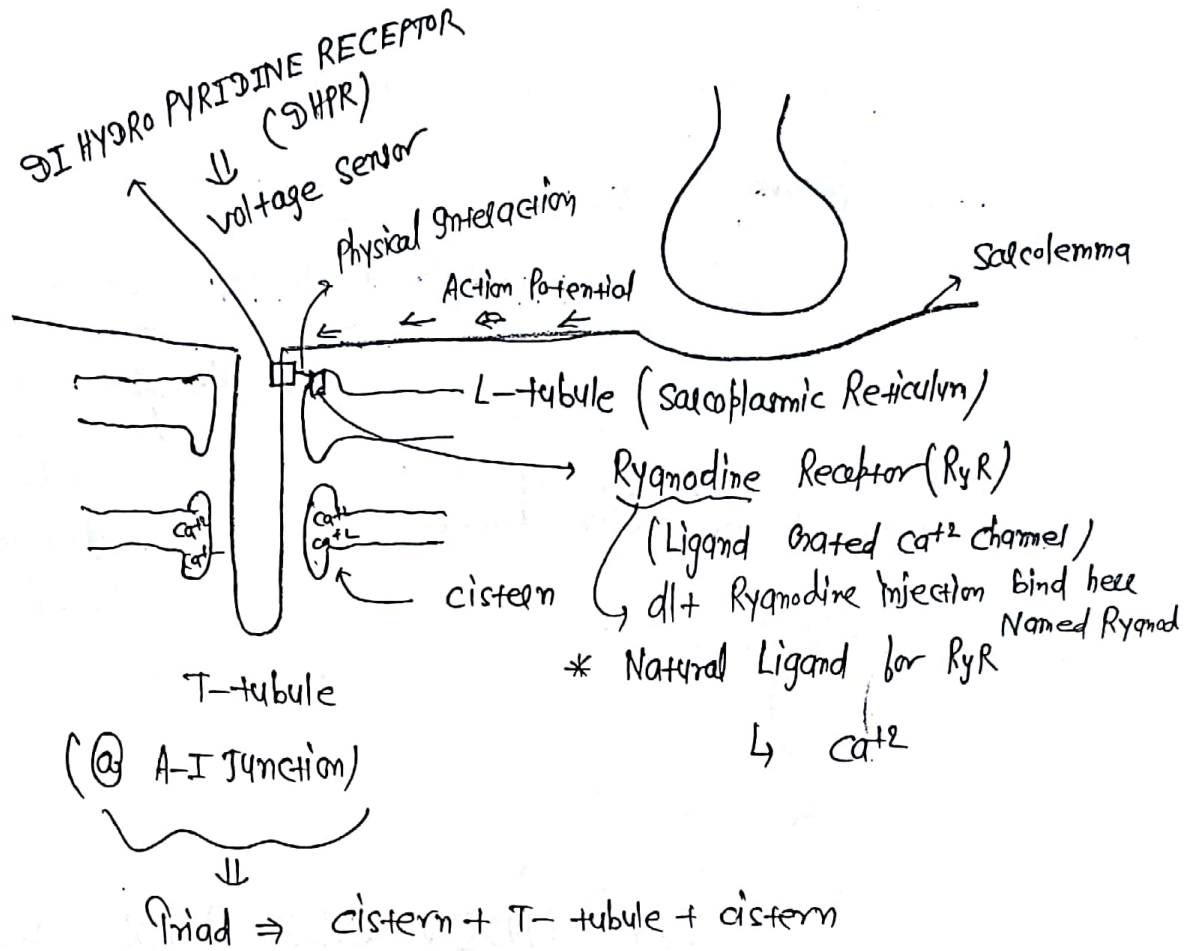
* NEUROMUSCULAR JUNCTION



LAMBERT EATON SYNDROME \Rightarrow Ab against Pre-synaptic voltage gated
 Ca^{++} channel

MYASTHENIA GRAVIS \Rightarrow Ab against Post-synaptic Ligand gated
 Na^+ & K^+ channels

SARCOTUBULAR JUNCTION



* as DHPR get conformational change
 ↓
 RyR gets interaction c DHPR & Release Ca^{2+}
 ↓
 K/as " Ca^{2+} induce Ca^{2+} Release"
 EXCITATION-CONTRACTION COUPLING
 Agent $\Rightarrow Ca^{2+}$

QA

* Trigger for Muscle Contraction \Rightarrow Availability of Sarcoplasmic Ca^{2+}

Q9

Muscle contraction continues till \rightarrow

a) ~~Ca^{+2}~~ is available;

b) ATP is available;

Q10

Relaxation of Muscle by \rightarrow

Removal of Salcaplasmic Ca^{+2}

\rightarrow by 1^o Active transport

\rightarrow through SERCA

Each ATP \rightarrow by hydrolyze $2ATP^{+2}$

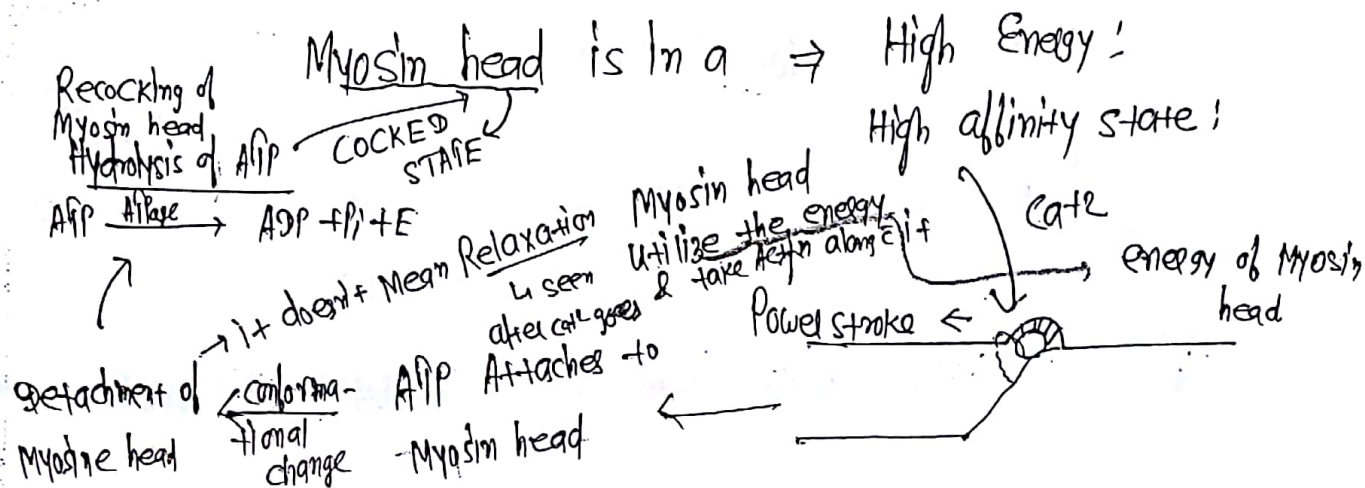
Goer into Salcaplasmic Reticulum.

\rightarrow So, it is active process.

ACTIN - MYOSIN CROSS BRIDGE CYCLING

- Responsible for sliding filament theory of Muscle contraction.

* When a Muscle @ Rest \Rightarrow



Sequence \Rightarrow

Power stroke



ATP attaches to Myosin head



Detachment of Myosine head



Hydrolysis of ATP



Recocking of Myosine-head,

* In Rigor Mortis Case \Rightarrow Cell Membranes become leaky



Ca^{+2} comes out of Sarcoplasmic Reticulum & comes in Sarcoplasm.



but there is No ATP to go inside the Sarcoplasmic Reticulum

Result in contracted state \leftarrow

* Only 1 ATP Requires in Actin - Myosin cross-bridge cycling

TYPE - I Muscle fibres

Type-I

S → Slow, Small

O → oxidative

R → RED

R

Y

QQ

Faster Myosin ATPase Activity ⇒ II

QQ

Longer twitch duration ⇒ I

QQ

Having More Mitochondria ⇒ I

QQ

Higher cap. Density ⇒ I

QQ

More myoglobin ⇒ I

QQ

Early fatiguability ⇒ II

I

↓

Slow; Sustained
contraction

Type-II

Fast; Large QQ

Glycolytic

White

II

↓

Brief powerful contr.

* Size principle ⇒ During Muscle contraction (Graded)

↓

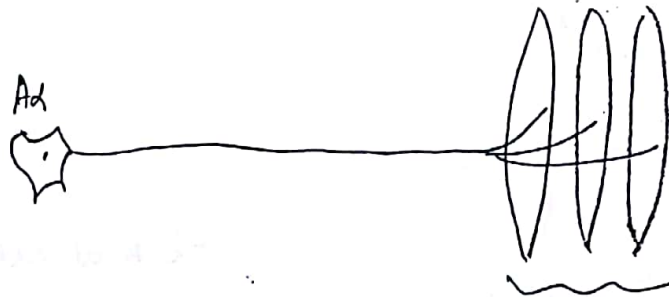
1stly Type-I muscle
fibres comes

→ then

Type-II muscle
fibres comes

(so: Reserve muscle
fiber)

MOTOR UNIT \Rightarrow Single Ax Motor Neurons + all Muscle fibres it supplies. (eg)



ONLY one type of Muscle fibres
in one Motor Unit.

Extraocular Muscle \Rightarrow Very fine control Needed
 \Downarrow
4-5 Muscle fibres / Motor Unit

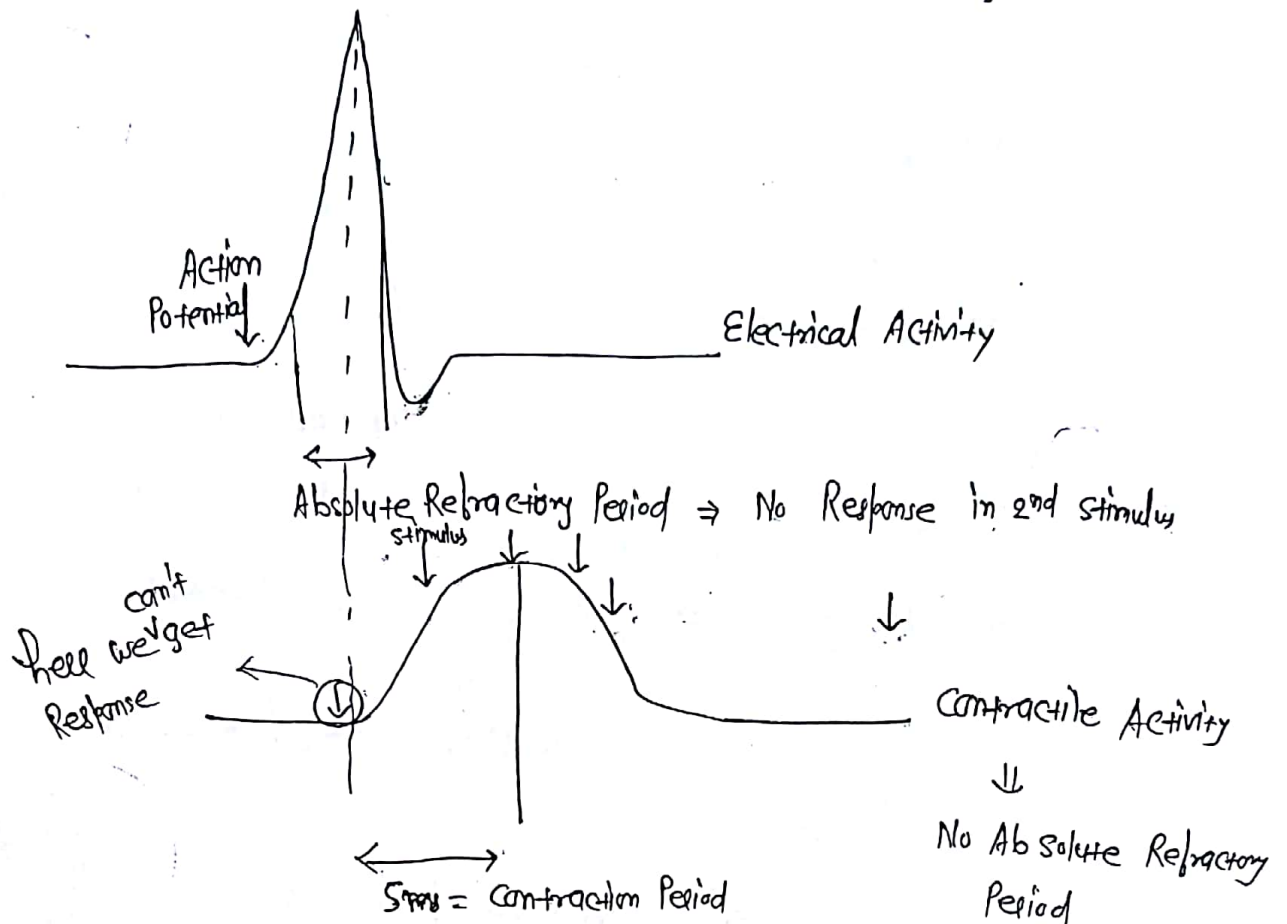
Muscles of Back \Rightarrow No need of fine control
 \Downarrow
600 Motor fibres / Motor Unit.

* Nomenclature of Motor Unit \rightarrow

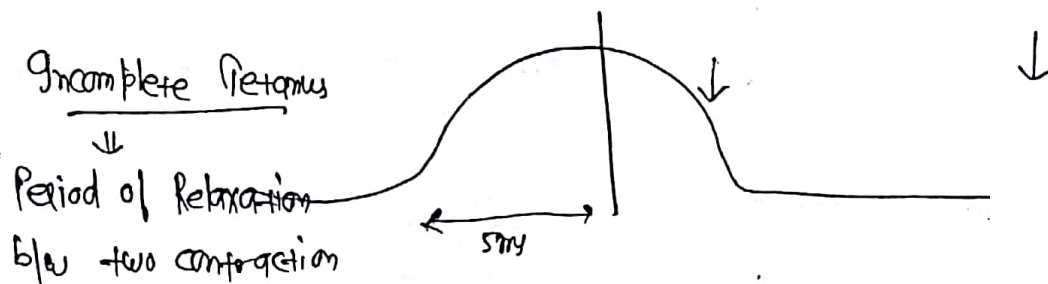
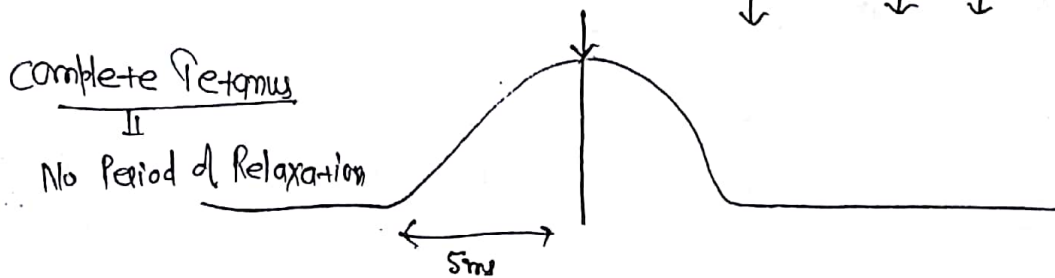
	I	IIa	IIb
<u>M. fibres</u>	Slow; oxidative (SO)	Fast; oxidative; Glycolytic (FOG)	Fast; Glycolytic (FG)
<u>Motor Unit</u>	(S) Slow	(FR) Fast & Resistance to fatigue	(FF) Fast & fatigable
eg \therefore	Standing \Downarrow "S" Motor Unit of calf Muscle	Walking \Downarrow "S" Motor Unit + "FR" Motor Unit	Running \Downarrow S + FR + FF Motor Unit

*

COMPLETE & INCOMPLETE TETANUS



Tetanus \Rightarrow State of continuous contraction.



(43)

⇒ In Successive Stimulation ↑ Height of Successive Contraction

↓

Klas "Beneficial effect/ staircase/ Treppe"

↓

d/t accumulation of the Ca^{2+} in S

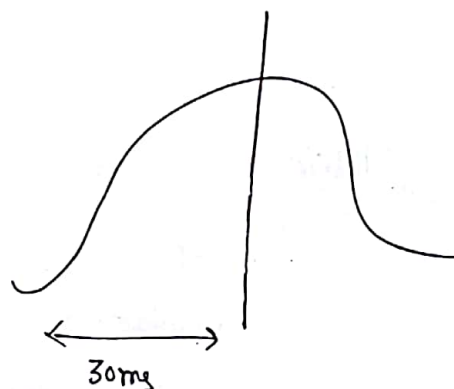
TETANIZING FREQUENCY ⇒ $\frac{1}{\text{Contraction Period (in sec)}}$

z $\frac{1}{5 \text{ ms}} = \frac{1000}{5} = 200 \text{ Stimuli/sec.}$

$= 200 \text{ Hz.}$

- * if frequency of stimulation is $> 200 \text{ Hz} \Rightarrow$ complete tetanus
- * if frequency of stimulation is $< 200 \text{ Hz} \Rightarrow$ incomplete tetanus

QA



Tetanzing frequency

↓

$\frac{1000}{30} = 33.33 \text{ Hz.}$

- * Day-to-day activities can't possible without Tetanus.

TYPES OF MUSCLE CONTRACTION

ISOTONIC

Tone | Tension = Same

Length = \downarrow es

External work = done

Heat Release = More

eg \Rightarrow all day-to-day activities

ISOMETRIC

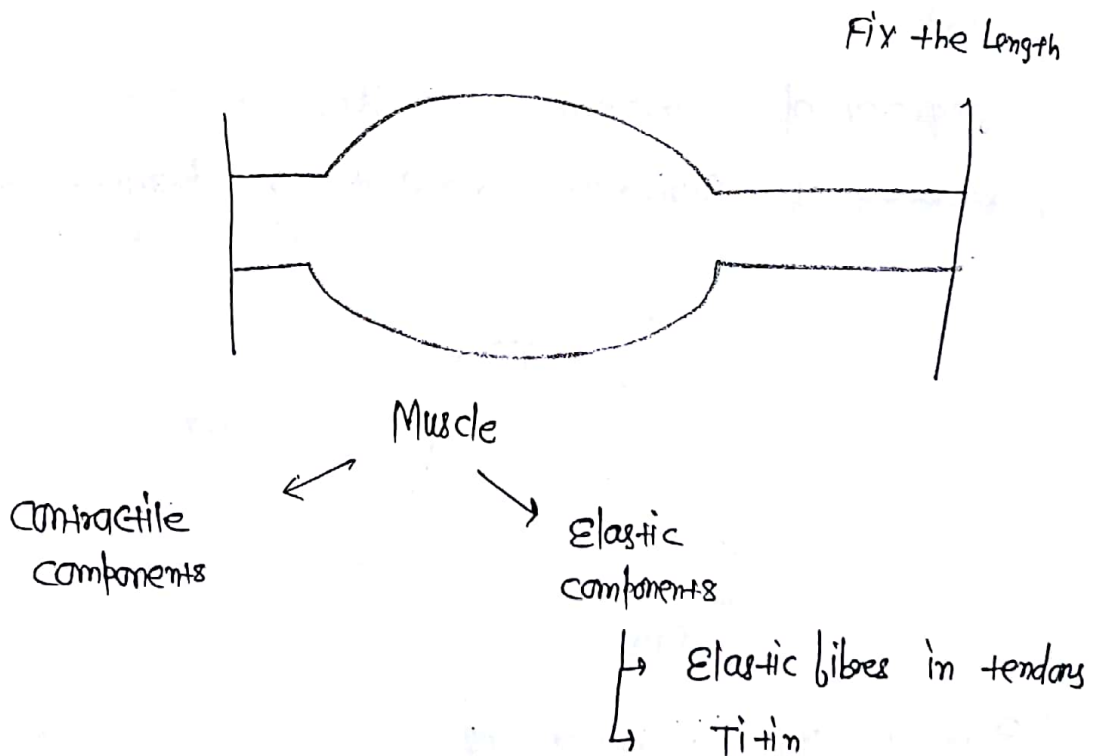
Length = Same

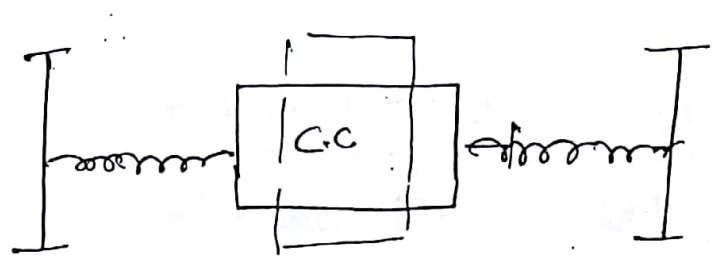
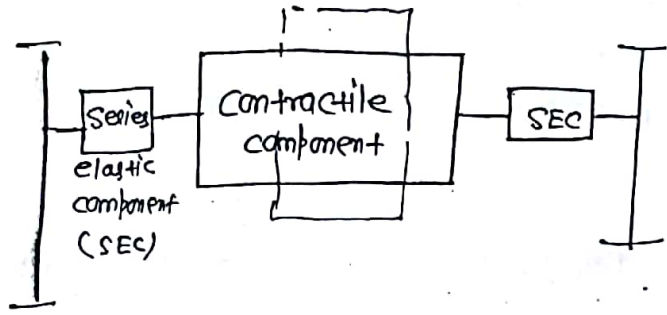
Tension = \uparrow

No External work

eg \Rightarrow Place hand on wall & push against it.

How does isometric contraction takes place ??

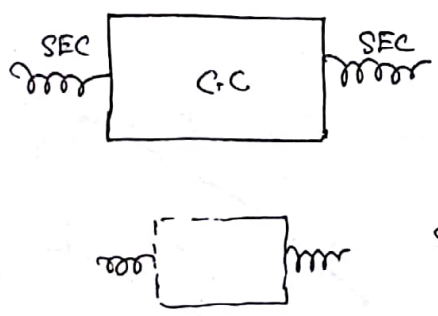




ISOMETRIC
↓

- ↓ Contractile component
- Stretch of series elastic component
- Total Length = Same

In Isotonic contraction ⇒



ISOTONIC

- ↓ Contractile component
- Series elastic component
↓
Folded

HEAT RELEASED DURING MUSCLE CONTRACTION.

ISOTONIC

ISOMETRIC

- i) Resting heat ⊕
- ii) Initial heat
 - ↳ Activation heat ⊕
 - ↳ Shortening heat ⊕
- iii) Recovery heat (stop giving stimulus & heat generated by muscle) ⊕

- ⊕
- ⊕
- ⊕
- ⊕

iv) Relaxation Heat \Rightarrow \oplus

\ominus

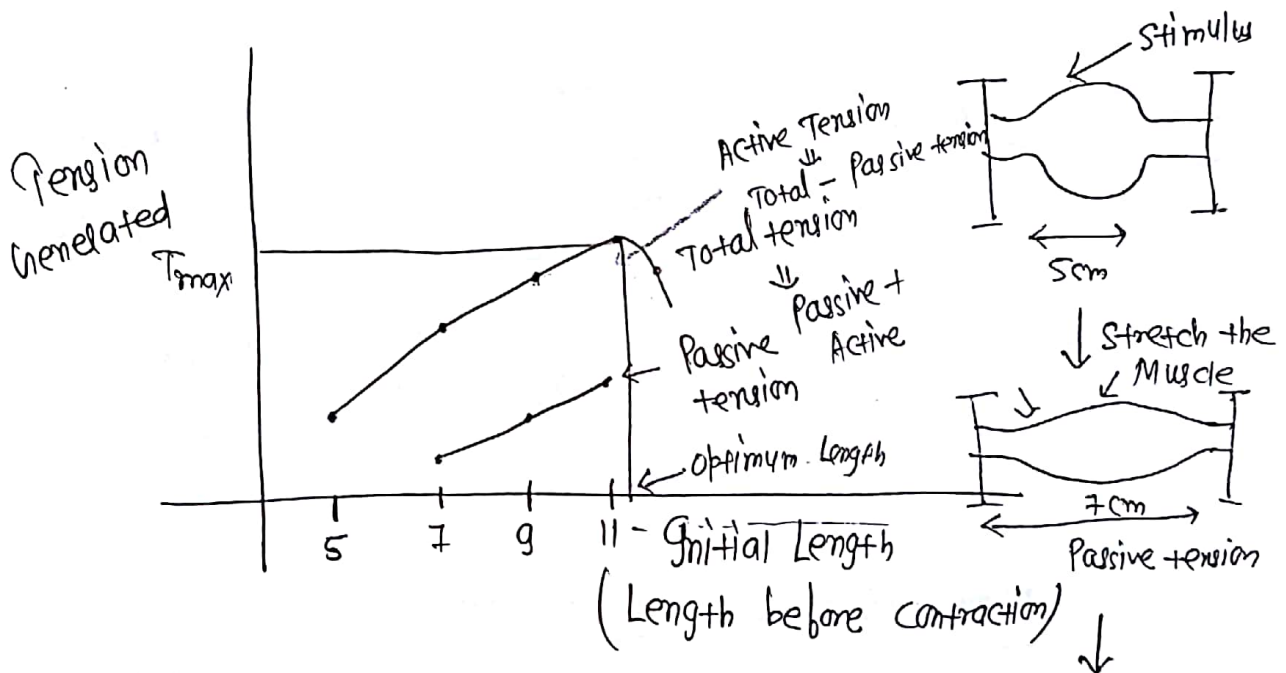
\uparrow Q (Total heat)

* Total heat generation is more in \Rightarrow Isotonic contraction

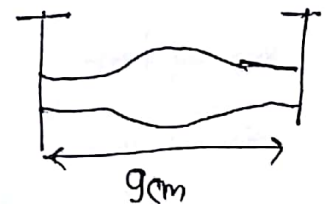
LENGTH-TENSION RELATIONSHIP

FRANK - STARLING'S LAW

— Applicable for isometric contraction; Not for isotonic contraction



during isometric muscle contraction; More the Initial Length; More is the total & Active tension generated; but upto a Physiological Limit; beyond which further rise in Initial Length; less the total & active tension generated



In case of cardiac Muscle →

(45)

⇒



↑ Venous Return

↓

↑ Filling (↑ End diastolic volume)
↳ Preload

↓

↑ Initial Length

↓

↑ Tension generated

↓

↑ Stroke volume

↑ Cardiac output ⇐
but up to physiological
Limit.

In Dilated cardiomyopathy ⇒

↑↑↑ Initial Length

↓

↓ Tension generated

↓

↓ stroke volume ⇒ Failure (common)

Optimum Length ⇒ It is that Initial Length; at which if Muscle contracts isometrically; then the total & active tension generated is maximum.

QA

At optimum Length; All are Max^m except ⇒

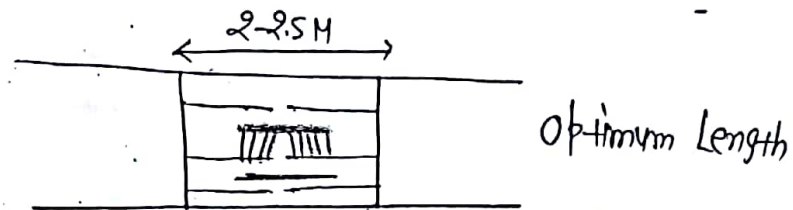
(A) Total tension;

(B) Active tension;

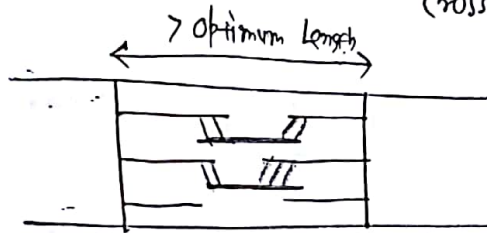
(C) Passive tension

Optimum Length \Rightarrow Corresponds to Sarcomere Length of 2-2.5 μ m

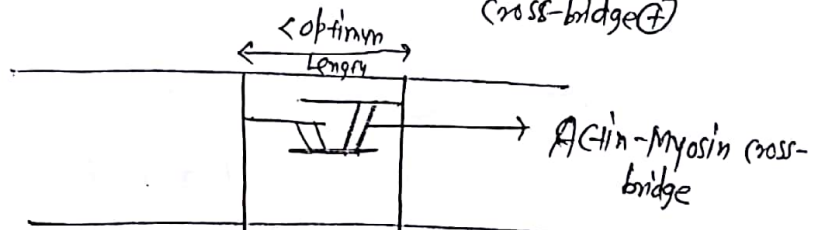
- ↳ Maximum overlap b/w Actin & Myosin
- ↳ Maximum Number of Actin-Myosin cross bridges
- ↳ also k/as "Resting Length".



ii) Initial Length is More than optimal Length \Rightarrow Less Actin-Myosin cross-bridge (+)



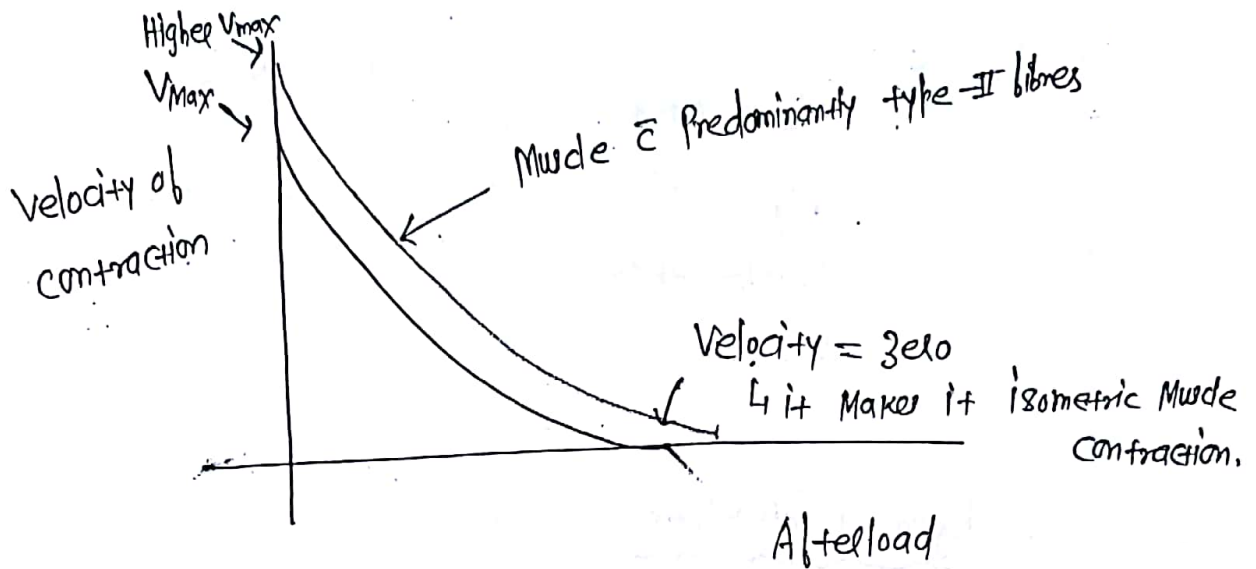
ii) Initial Length is Less than optimal Length \Rightarrow Less Actin-Myosin cross-bridge (+)



LOAD-VELOCITY RELATIONSHIP

9/14/21

- Valid for Isotonic Muscle



Afterload for the heart \Rightarrow Total Peripheral Resistance

* SOURCES OF Energy during exercise \Rightarrow

1. ATP Stores \Rightarrow Sustain the exercise for 1-2 sec only
 \Downarrow
 1st source of energy
 In Trained Athletes \rightarrow 3 sec

2. ATP from creatine phosphate \Rightarrow Sustain the exercise for 7-8 sec

Klas "Phosphagen system"

\hookrightarrow Sustain 8-10 sec

3. ATP from Glycolytic Metabolism \Rightarrow Sustain the exercise for 1-1.5 min

4. ATP from oxidative Metabolism \Rightarrow Sustain for Long time

Energy Substrate \Rightarrow 1st Stored Glycogen \rightarrow Glucose \rightarrow Fatty acid
 \hookrightarrow After 1st 2 mins of exercise

* Phosphagen system (Major Source) →

For 100 metre sprint

Diving

Long jump

High jump

Javelin throw

Discus

* Phosphagen + Glycolytic →

200 metre Run ;

100 m Swim ;

* Glycolytic →
(Major Source)

400 m Run

200 m Swim

* Oxidative →

For Any Prolonged duration of exercises

- Marathon

- Boxing

- Rowing

TRAINING OF ATHLETES

ENDURANCE TRAINING

⇒ ↑ Stamina

⇒ ↑ Efficiency of CVS & Respiratory
System to tolerate exercise

STRENGTH TRAINING

⇒ ↑ Strength/Power

⇒ ↑ Bulk of Muscle
(Hypertrophy)

⇒ Load ⇒ Submaximal
Duration ⇒ Prolonged

⇒ Test oxidative capacity

⇒ Achieved by ⇒ Walking
Jogging
Swimming

⇒ Load ⇒ Maximal OR
Near Maximal
Duration ⇒ Brief

⇒ Test Glycolytic capacity

⇒ Achieved by ⇒ Training;
Gymming

QA CARDIOVASCULAR SYSTEM

Cardiac Muscle \Rightarrow

Striated

Involuntary Muscle

Extensive branching

Intercalated Discs

At Z-line

↑ Cell - to - cell cohesion

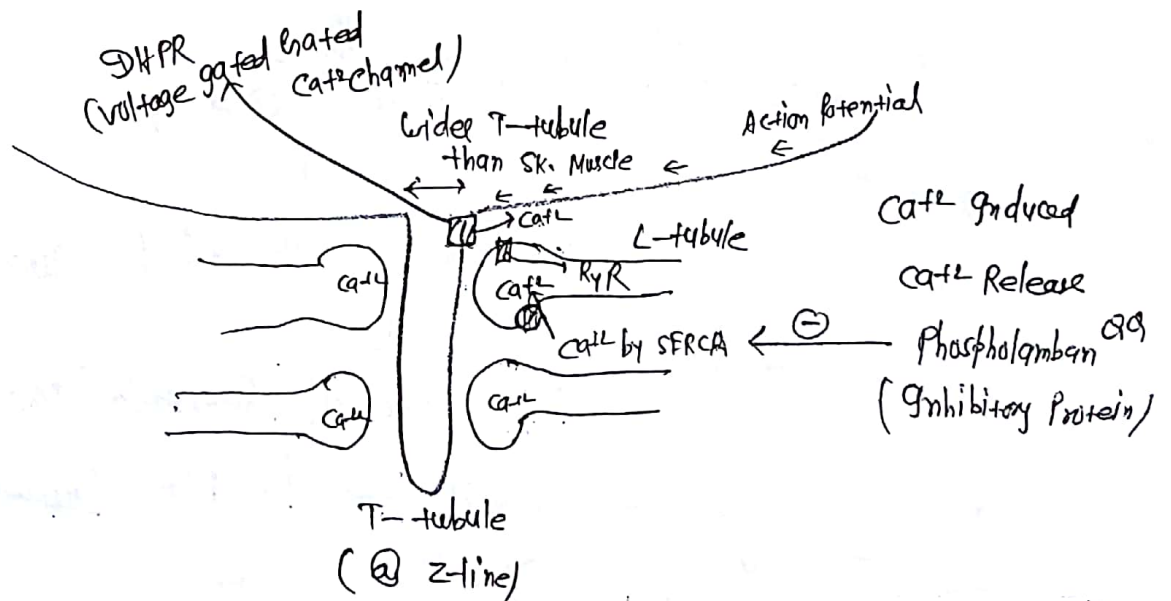
↓ it heart is "Mechanical syncytium"

Gap Junctions \oplus

At Z-line

↓ it heart is "Functional syncytium"

*



Skeletal Muscle

Cardiac Muscle

T-tubule \Rightarrow

A+ A-I Junction

A+ Z-line

Sarcoplasmic Reticulum \Rightarrow

Better developed

Source of Ca^{2+} \Rightarrow

SR

ECF + SR

DHPR \Rightarrow

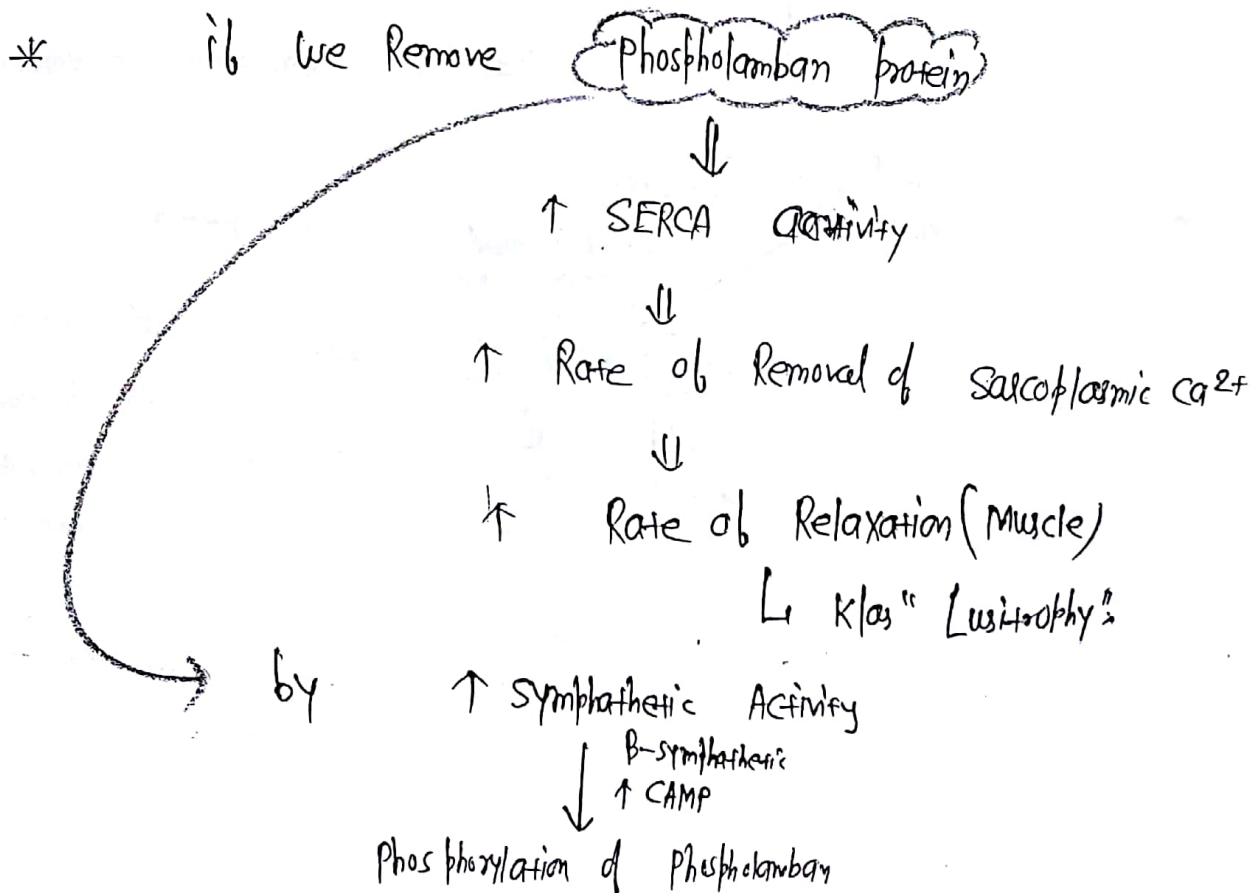
Voltage Sensor

Voltage gated Ca^{2+} channel

Relaxation \Rightarrow

SERCA

SERCA +
Na⁺- Ca^{2+} Antiport



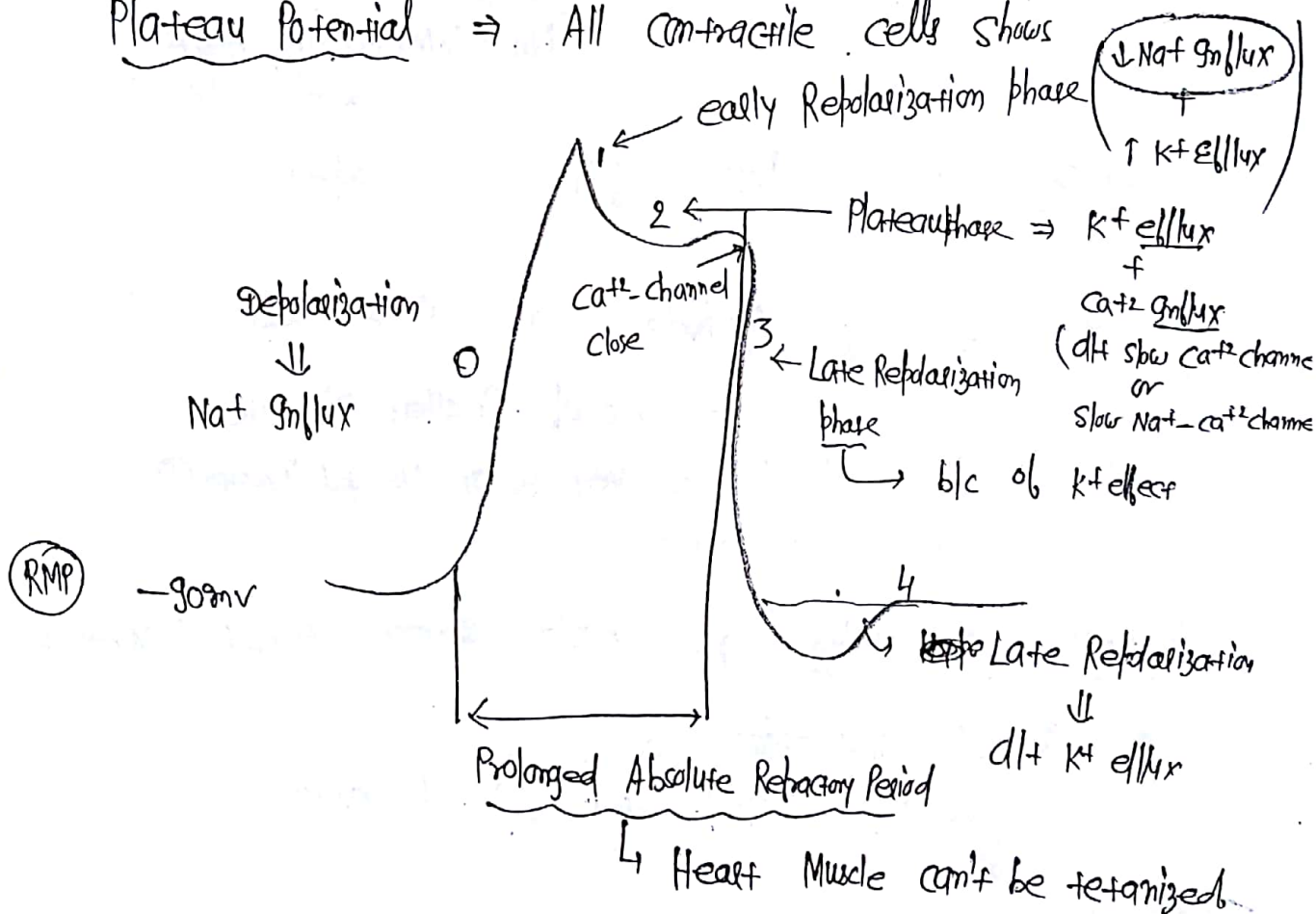
* ↑ Sympathetic ⇒

(99)

- ⊕ve Chronotropic (↑ Heart Rate)
- ⊕ve Inotropic (↑ Force)
- ⊕ve Bathmotropic (↑ Excitement)
- ⊕ve Dromotropic (↑ Conductivity)
- ⊕ve Lusitropic (↑ Muscle Relaxation)

* Electrical Activity of Heart ⇒

Plateau Potential ⇒ All contractile cells shows

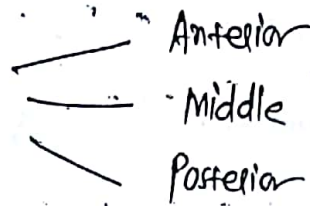


* conducting system of Heart \Rightarrow

Modified contractile cells.

i) SA Node

ii) Inter Nodal tracts



iii) AV Node \Rightarrow Nodal delay (as it passes through AV Node it slow)
 $92 \text{ ms} = 0.092 \text{ sec}$

iv) Bundle of His

v) Bundle Branches



vi) Purkinje fibres

No NMJ \oplus in Heart,

Fastest \Rightarrow

Purkinje fibres $\Rightarrow 4 \text{ m/sec}$

Slowest
conducting \Rightarrow

AV Node $\Rightarrow 0.05 \text{ m/sec}$

\hookrightarrow b/c of Smallest Diameter
& very few or No gap junction \oplus .

Advantage of Nodal delay \Rightarrow

Atria contract Ahead of ventricle

* Atrial contraction

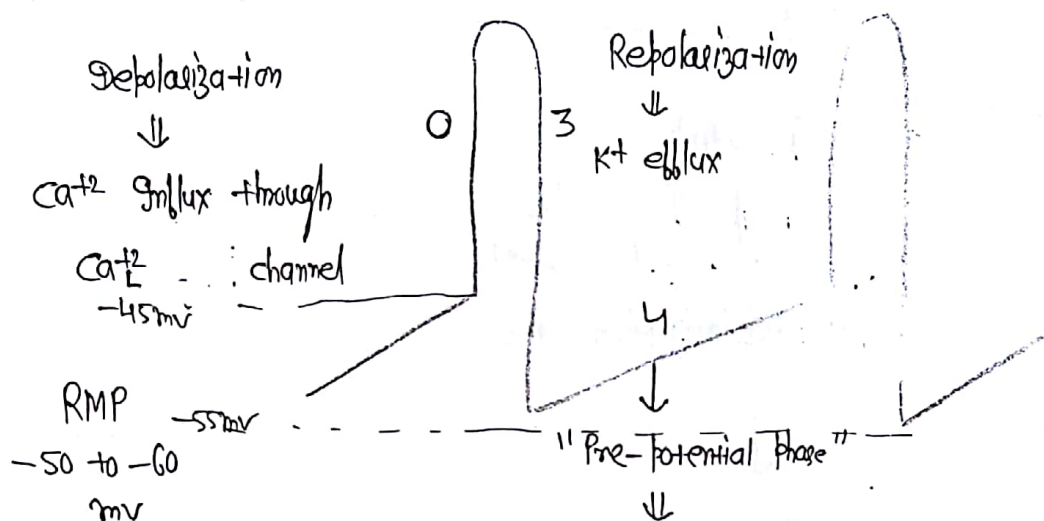
Responsible \hookrightarrow 2nd Rapid filling of ventricle
for

Pacemaker Potential \Rightarrow (a) SA Node
& AV Node

(50)

All of Rest have "Plateau potential"
 \Downarrow
 eg = Bundle of his; Purkinje cells \rightarrow also in contractile cells.

PACEMAKER POTENTIAL

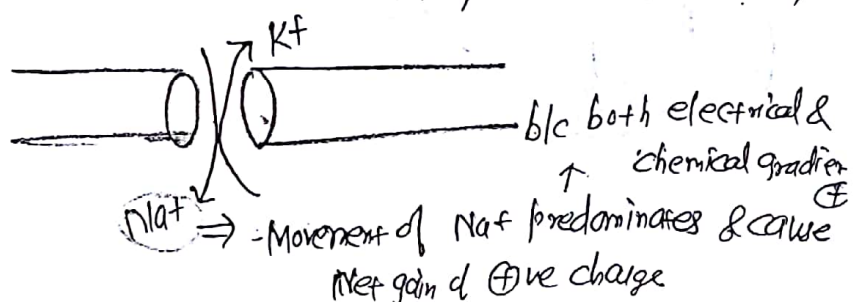


"Spontaneous depolarizing till firing level"

by gain of \oplus ve charge

① by \downarrow K^+ efflux

② by opening of "F" channel (it permits movement of both Na^+ & K^+)
 \hookrightarrow Funny



③ Ca^{+2} influx through Ca_T channels

Q9 Pre-potential starts \bar{c}
↳ ↓ in K^+ efflux

Main Reason for Pre-potential

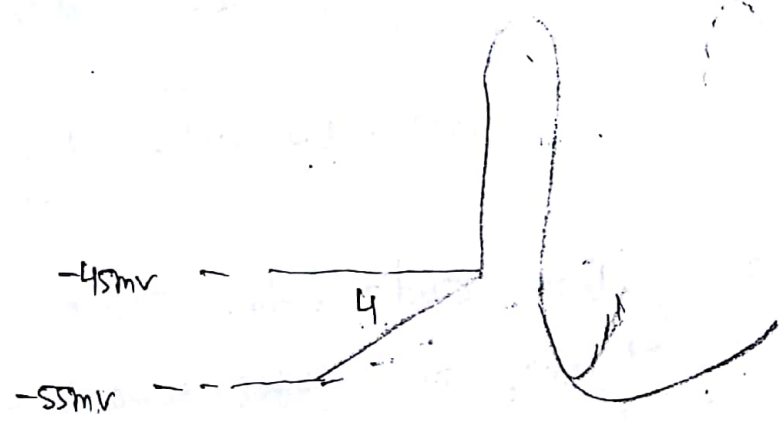
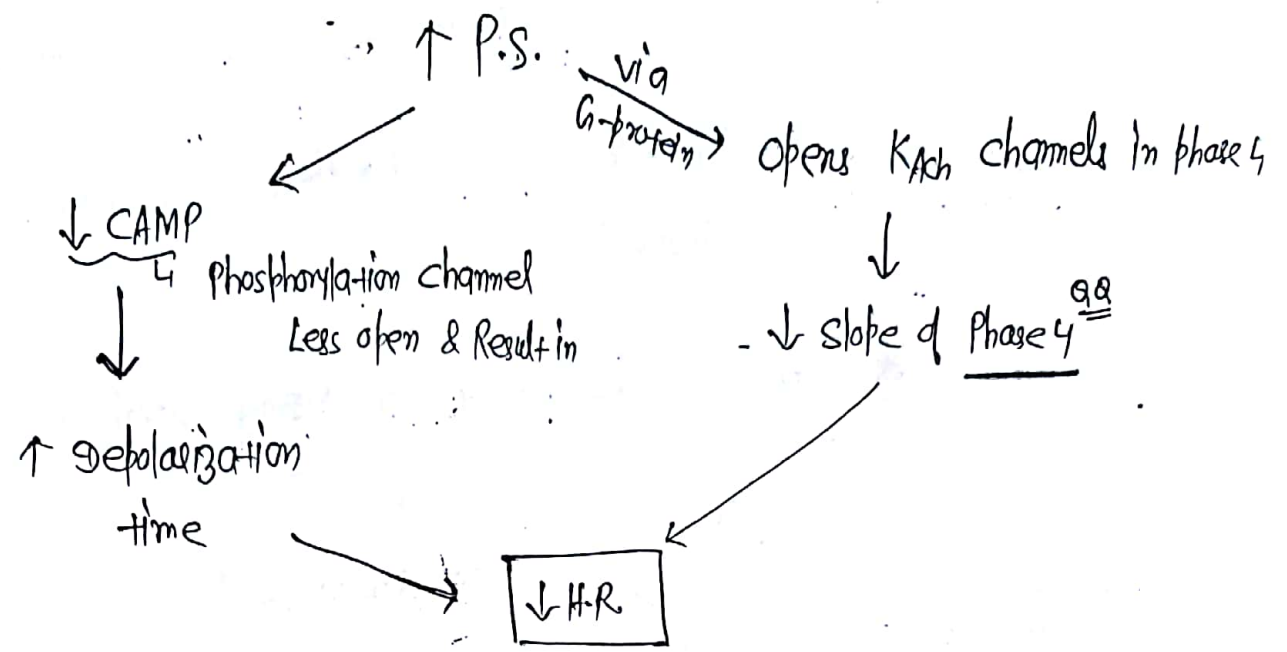
↳ Ca^{+2} influx through Ca_T channels

*

Effect of Sympathetic discharge on Pacemaker Potential

↑ Symp.
↓ β Receptor
(↑ cAMP)
↓ Depolarization time
↓
↑ HR

* Effect of Parasympathetic discharge on Pacemaker Potential



QA Parasympathetic affects Phase 4 & 0 both.

* Intrinsic Rate of discharge of SANode] $\rightarrow 100/\text{min}$
 \downarrow b/c of Resting vagal tone
 Resting heart Rate $\rightarrow 70-80/\text{min}$ i.e vagus is effective @ Rest

Q8

Heart Rate of Transplanted Heart

↳ 100/min (No connection to Sympathetic & Parasympathetic)
↳ In exercise; epinephrine from Adrenal Medulla works here

Athletes \Rightarrow has very high Resting Vagal tone



Bradycardia @ Rest

\hookrightarrow Advantage \Rightarrow High Cardiac Reserve



Max cardiac output - Basal cardiac output

In (N) Individual \Rightarrow
4-5 times rest

Basal cardiac output = 5 L/min

Max cardiac output = 20-25 L/min

In Athletes \Rightarrow

Basal cardiac output = 4.0 L/min



6-7 times rest

Max cardiac output = 25-28 L/min

Rt. Vagus

SA
Node

Lt. Vagus

AV
Node

Overlap++

*

Sympathetic

Heart Rate

↑

Force of contraction

↑

Parasympathetic

↓

⊖

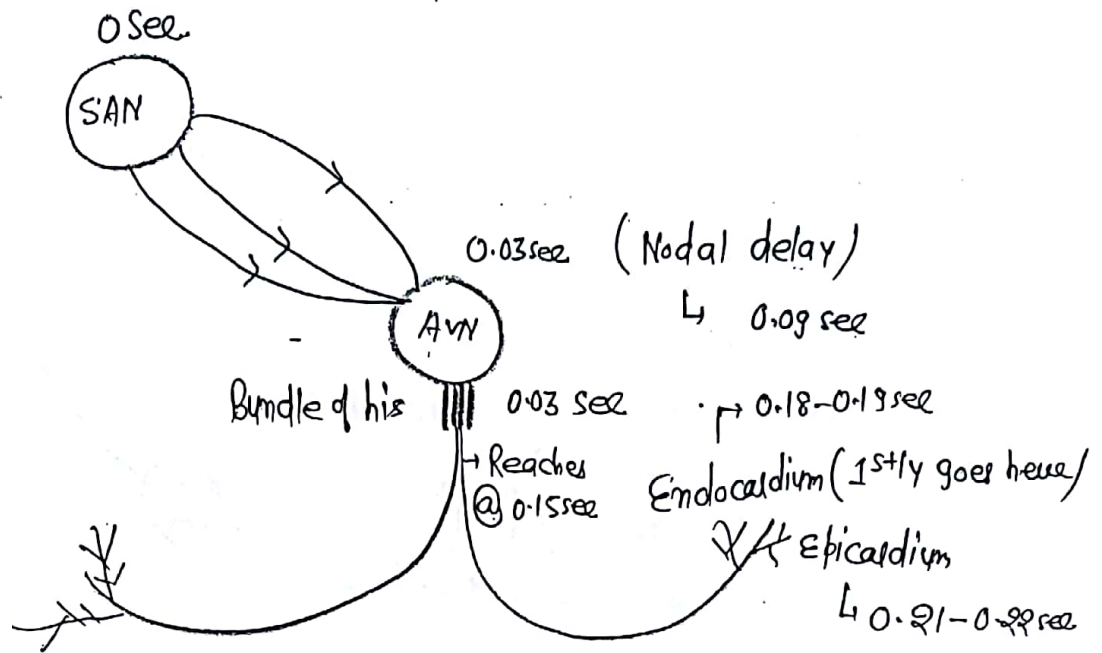
(No vagus to ventricle)

==

Parasympathetic is pr. in all except

- a) SAN;
- b) AVN;
- c) Atrial Myocardium
- d) Ventricle Myocardium

CONDUCTION OF CARDIAC IMPULSE



VENTRICLE DEPOLARIZATION

1st to depolarize ⇒ Left upper part of Interventricular Septum



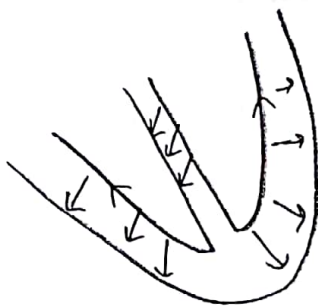
Septal depolarization (Left → Right)



Endocardium then Epicardium (2016 NEET)



Last to depolarize ⇒ Base of heart (Epicardium)



- Pulmonary Conus

- Small superior Most portion of Interventricular septum Near base of heart

* VENTRICULAR REPOLARIZATION ⇒

(53)

1st part to Repolarize ⇒ Apex; Epicardium

Last part of Repolarize ⇒ Base; Endocardium

* During Repolarization Heart is already in contracted state



there is very high pressure in Endocardium (b/c of circular Nature)



This high pressure doesn't permit ionic change

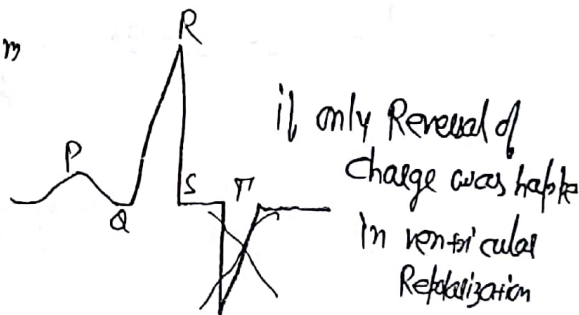


Repolarization is from Epicardium → Endocardium

Q. Isolated piece of vent. Myocardium



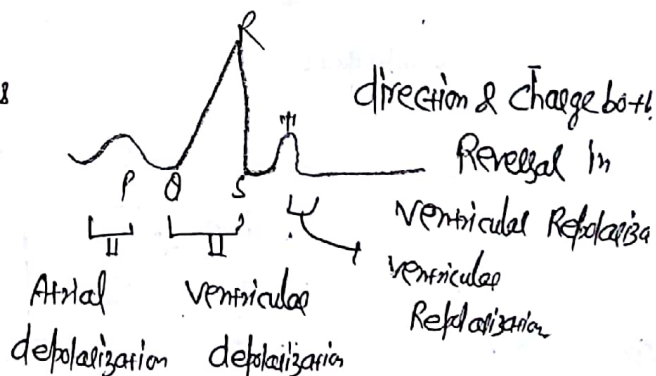
Shows both electrical activity & conduction activity



Repolarization is from ⇒ both surface has

a) Endo → Epi equal pressure

b) Epi → Endo

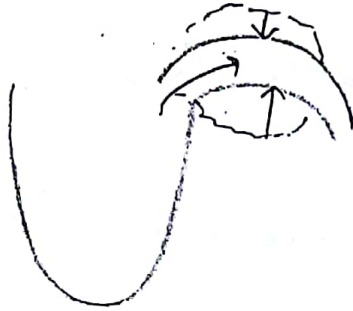


VESSELS

1. WINDKESSEL VESSELS

↳ Aorta & Large Arteries

Elastic tissue ++



during diastolic

↳ diastolic Blood Pressure



↳ Elastic Recoil of Aorta & Large Arteries;

↳ depend on Total Peripheral Resistance

2. Resistance vessels

↳

↳ least of blood volume
Arterioles (only 1% of TBV pr. here).



Smooth Muscle ++

Sympathetic ++

↑ Sympathetic Innervation d/t more Smooth Muscle



Vasomotor contraction



↓ Radius



↑↑↑ Resistance

$$R \propto \frac{1}{r^4}$$

↳

Small change in Radius

↳ Large change in Resistance

③ Exchange vessels

⇒

Capillaries

⑤4



No Smooth Muscle

No Sympathetic Innervation

4 ~ 5% of total blood volume

* Pre-capillary sphincters
&
Terminal Arterioles

Respond to
Local Metabolite



↓ P_{O_2}

↑ P_{CO_2}

↑ H^+

↓ pH

↑ Lactic acid

↑ Adenosine

↑ temp.

↑ K^+

Local
hypoxia

⇒ causes Relaxation of pre-
capillary sphincters & terminal
arterioles.



↑ capillary flow.

o₂ sensitive
K⁺ channel
Pulmonary → ↓ P_{O_2}
↓
Vasoconstriction

↓ P_{O_2}



Closure of O₂-sensitive
K⁺ channel



↓ K^+ efflux



Depolarization

↳ Vasoconstriction

ATP dependent K⁺
channels → Vaso dilation
(Rest all area)

↓ P_{O_2}



↓ ATP



Opening of ATP dependent K⁺ channels



↑ K^+ efflux



Hyperpolarization ⇒ Vasodilation

#

Resting Skeletal Muscle blood flow

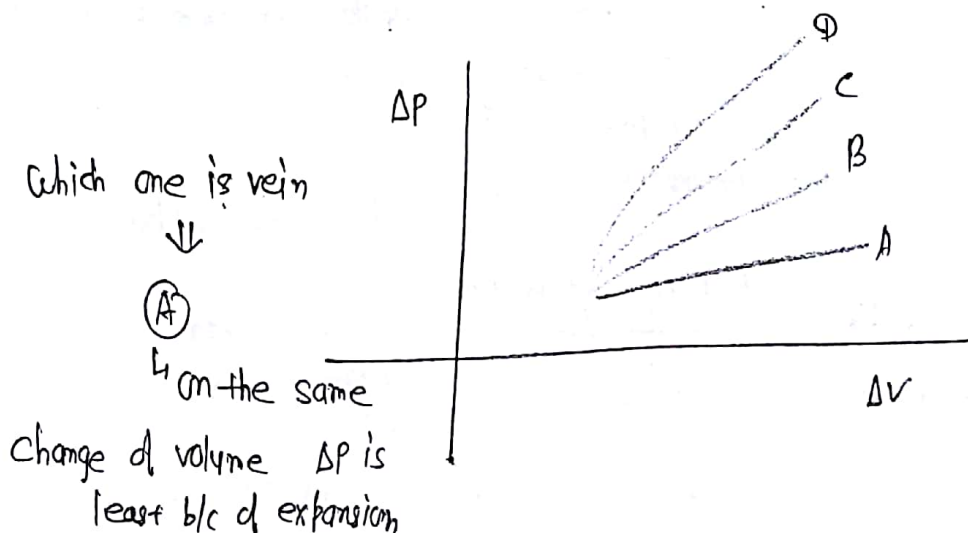
3-4 ml/min/100 gm of tissue

On Exercise / Local Metabolites (20-25 times)

80-90 ml/min/100 gm of tissue

④ CAPACITANCE VESSELS \Rightarrow Venules; Veins & Vena cava

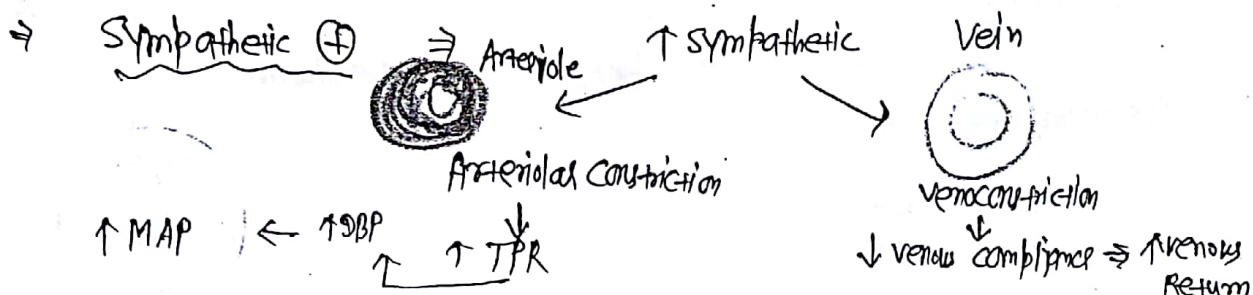
- ↳ \sim 2/3rd of blood volume prts on venous side (60%)
- ↳ have capacity to expand



compliance
 \downarrow
distensibility of vein

Small veins = 46% of blood volume

Large veins = 14-18% of blood volume



⑤ Shunt Vessels \Rightarrow Arterio-Venous Anastomosis (SS)

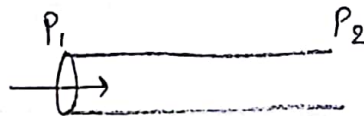
↳ pr. in Finger tips \oplus
Ear lobes \oplus
Function \Rightarrow Temperature Regulation.
Sympathetic supply \oplus

Imp.

HEMODYNAMICS

① Based on ohm's Law \Rightarrow

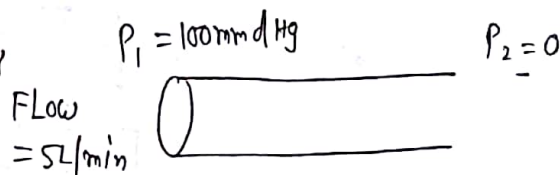
$$\text{Flow} = \frac{P_1 - P_2}{\text{Resistance}}$$



Flow $\propto \Delta P$

Flow $\propto \frac{1}{\text{Resistance}}$

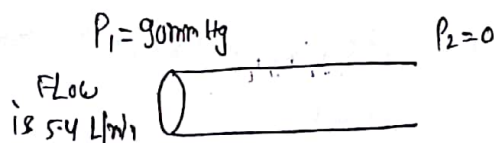
Q. Resistance in wood units?



$$\text{Resistance (Wood Units)} = \frac{\Delta P \text{ mmHg}}{\text{Flow L/min}} = \frac{100 - 0}{5} = \frac{20 \text{ mmHg/min/L}}{20 \text{ Wood Units}}$$

Q. Resistance in R Units?

(PRU)
Peripheral Resistance unit



$$\text{Resistance (PRU)} = \frac{\Delta P (\text{mm of Hg})}{\text{Flow (ml/sec)}} = \frac{90-0}{90} = 1 \text{ PRU}$$

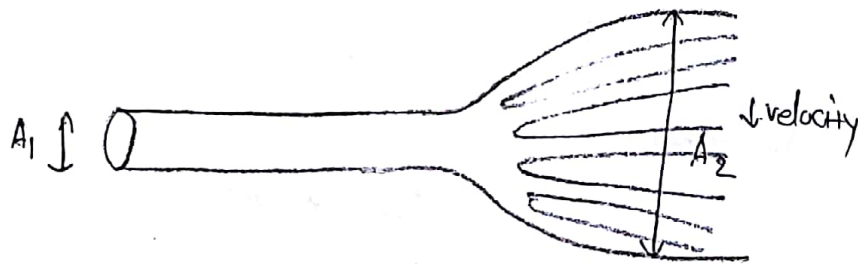
$9 \downarrow$
 $\frac{80 \times 1000}{60 \times 10} = 90$

② Velocity of Flow \rightarrow It is Inverse of total cross sectional Area

Aorta $\Rightarrow 4.5 \text{ cm}^2$ (Total cross-sectional Area)

Capillaries $\Rightarrow 4500 \text{ cm}^2$ (Total cross-sectional Area)

③ Max^m velocity \Rightarrow (a) Aorta



$$V_1 A_1 = V_2 A_2$$



$$V_1 A_1 = V_2 A_2$$

③ HAGEN - POISEUILLE'S LAW \rightarrow

η = viscosity (depend on RBC count)

L = Length

r = Radius

$$R = \frac{8\eta L}{\pi r^4}$$

We know;

(36)

$$\text{Flow} = \frac{\Delta P}{R} = \frac{\Delta P \times \pi r^4}{8 \eta L}$$

$$\text{Flow} = \frac{\pi}{8} \times \frac{\Delta P r^4}{\eta L}$$

$$\text{Flow} \propto \Delta P; \quad \text{Flow} \propto \frac{1}{\eta};$$

$$\text{Flow} \propto r^4; \quad \text{Flow} \propto \frac{1}{L}$$

In Anemia \Rightarrow blood viscosity \downarrow

\hookrightarrow Result in hyperdynamic circulation

QQ

Radius is res by 50% ; flow res by
~~a) 5x;~~ b) 8x; c) 10x; d) 16x

$$x + \frac{50}{100}x = \frac{3}{2}x$$

$$\frac{8x}{16} = 5 \text{ times}$$

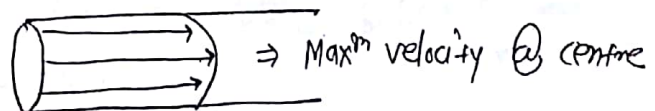
QQ

Radius & Length of a vessels are both double ; Flow res by
how many times

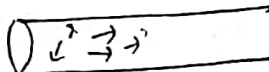
a) 5x; ~~b) 8x;~~ c) 10x; d) 16x

4) Laminar flow & Turbulent flow \Rightarrow

Laminar flow \Rightarrow



Turbulent flow \Rightarrow



Tendency for turbulence

→ Given by
Reynold's No.^{xx}

$$\Rightarrow \boxed{Re = \frac{\rho \cdot v \cdot d}{\eta}}$$

Most imp. factor

↳ velocity of flow

ρ = Density

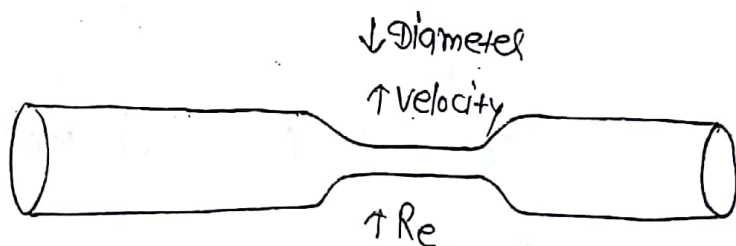
d = Diameter (cm)

v = velocity of flow (cm/sec)

η = viscosity (Poise)

$Re > 3000 \Rightarrow$ Turbulent flow

$Re < 2000 \Rightarrow$ Laminar flow



Korotkoff sounds

↳ heard diff turbulent flow

Seen turbulent flow

b/c velocity of flow is most important factor in Reynold's Number

⑤ Laplace's Law \Rightarrow

For thin walled vessels

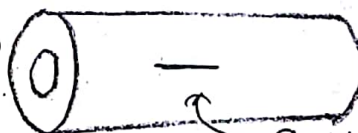


P = Distending Pressure

T = wall tension

$P = \frac{\pi}{r}$ (Cylinder eg Blood vessels)

$P = \frac{2\pi}{r}$ (Sphere eg Alveolus)



Incision & check wall tension

$T = Pr$

capillary \Rightarrow ↓ wall tension

- capillaries don't rupture despite of being thin walled

* if wall thickness (w) is significant \Rightarrow

(57)

$$T = \frac{Pr}{w} ; \quad T = \frac{Pr}{2w}$$

Q. Left ventricle wall stress (wall tension) can be \downarrow by \uparrow in \Rightarrow

a) Distending Pressure;

b) Radius

$$T = \frac{Pr}{2w}$$

\hookrightarrow In dilated cardiomyopathy patient there is less wall tension

c) Afterload (Total Peripheral Resistance)

~~d) wall thickness~~ \hookrightarrow In case of Heart.

⑥ FAHRAES - LINDQUIST Effect \Rightarrow

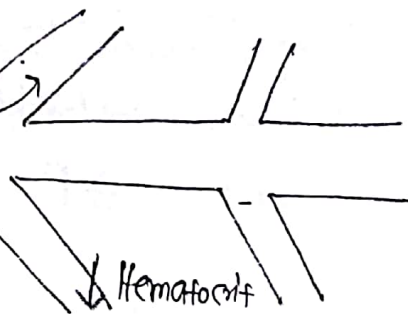
(Plasma Skimming)

RBC poor & Plasma-rich blood



RBC tends to occupy central

lastest moving stream of blood



Hematocrit

\downarrow Blood viscosity in vessels $< 1\text{mm}$ in diameter

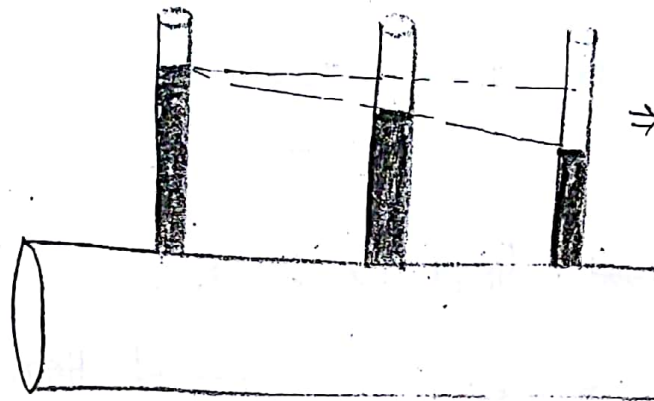
• It helps to maintain the flow

⑦

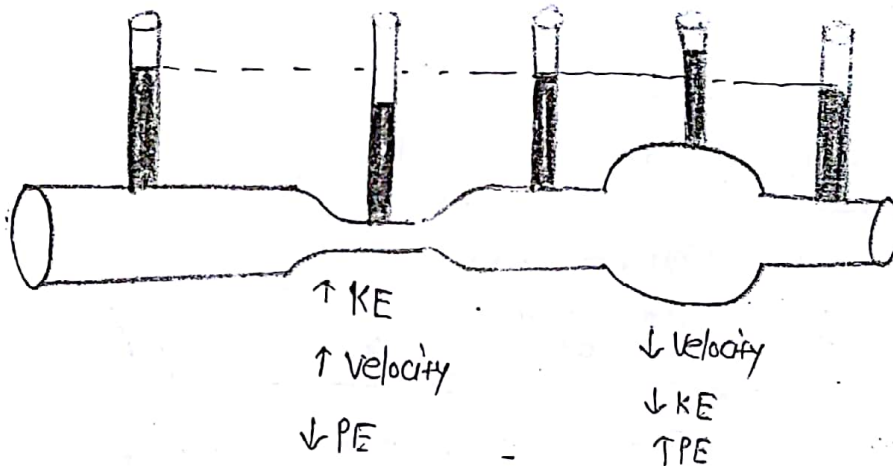
BERNOULLI'S \Rightarrow

Total energy = Kinetic energy + Potential energy

Total energy of Flow = Kinetic energy of Flow + Potential energy (Lateral pressure exerted by flowing bloods).

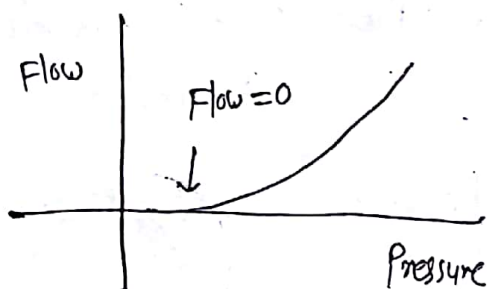


\Rightarrow \downarrow Lateral Pressure along Length of tube (b/c of loss of energy d/t friction)



⑧

Critical closing Pressure \Rightarrow

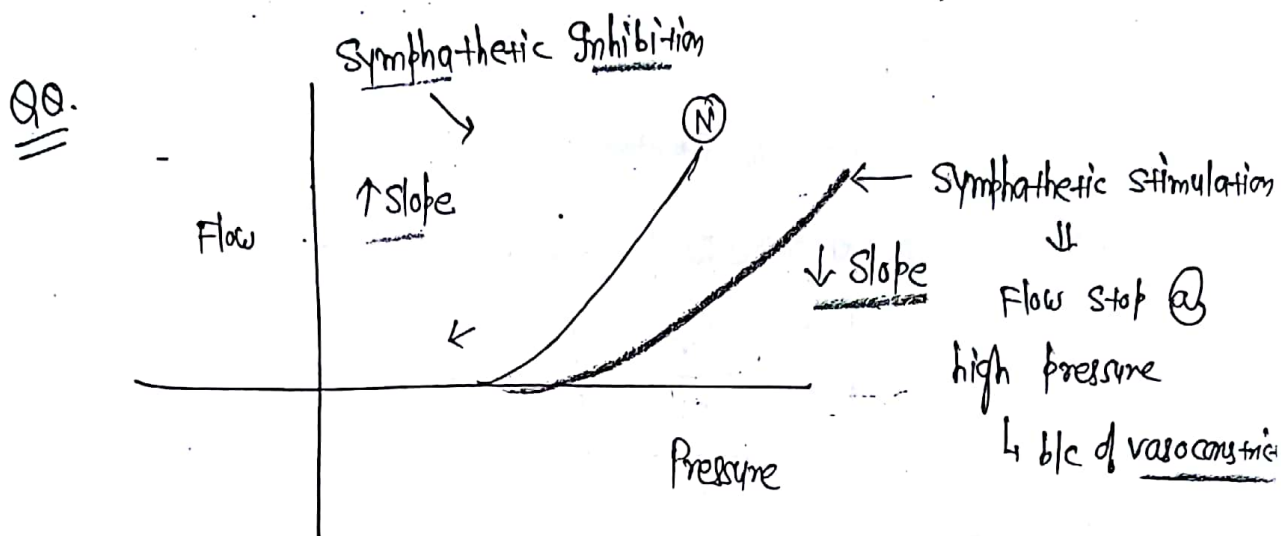


It is the pressure in small & thin walled vessels; when there is No Flow

Reason \Rightarrow i) Collateral inflow into the Arteriolar Meshwork;
ii) Rouleaux formation

iii) External Tissue Pressure > Distending pressure
Inside vessel.

iv) High Vascular Smooth Muscle tone
(eg in Arterioles)



* Parasympathetic Not seen @ blood vessels
few exception only.

MYOCARDIAL O₂ demand

- ↳ "Hard working organ"
- ↳ Oxidative Metabolism (< 1-f ⇒ Glycolytic)
- ↳ Fuel for heart -- Fatty acids

Q.Q. Basal O₂ demand ⇒ Quiescent heart
↳ 2 ml/min / 100 gm of tissue

Demand of Skeletal Muscle @ Rest ⇒ 0.2 ml/min / 100 gm of tissue

Beating heart @
Rest

\Rightarrow

9 ml/min/100 gm

* Factors for Myocardial O₂ demand \Rightarrow

① Heart Rate;

② Duration of systole;

③ Intra Myocardial tension

$$T = \frac{P_r}{2w}$$

④ Work done by heart = $\frac{\text{Stroke Volume} \times \text{Mean Arterial Pressure}}{\uparrow SV \quad \uparrow MAP}$
 \uparrow Vol. work \uparrow Pressure work
In AR In AS

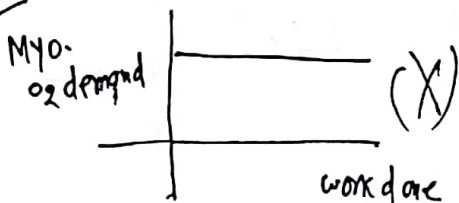
\uparrow O₂ demand \bar{c} \uparrow in pressure work is

\bar{c} in volume work

\Rightarrow In patient of AS higher O₂ demand than AR.

\downarrow
So; pt. of AS commonly presents \bar{c} Angina

Q.Q. Work done & Myo. oxygen demand = ~~constant~~ Relationship
Almost Linear Relationship



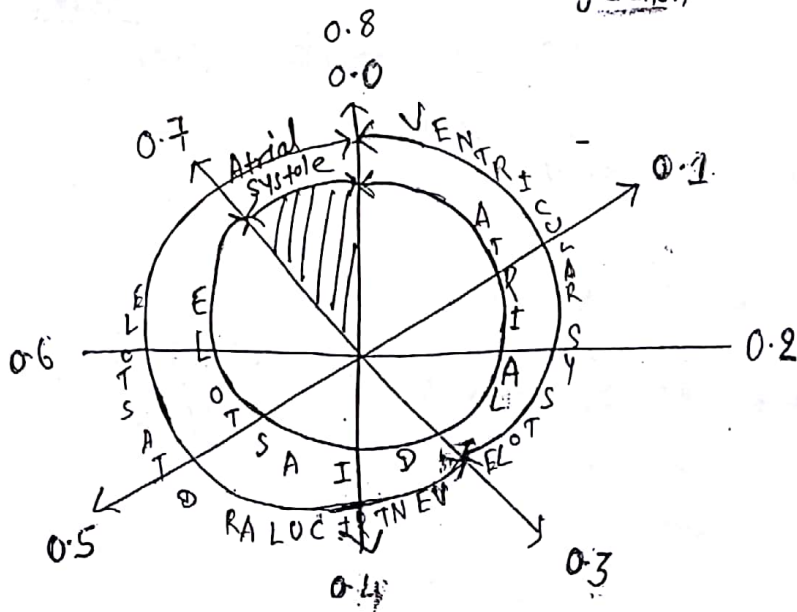
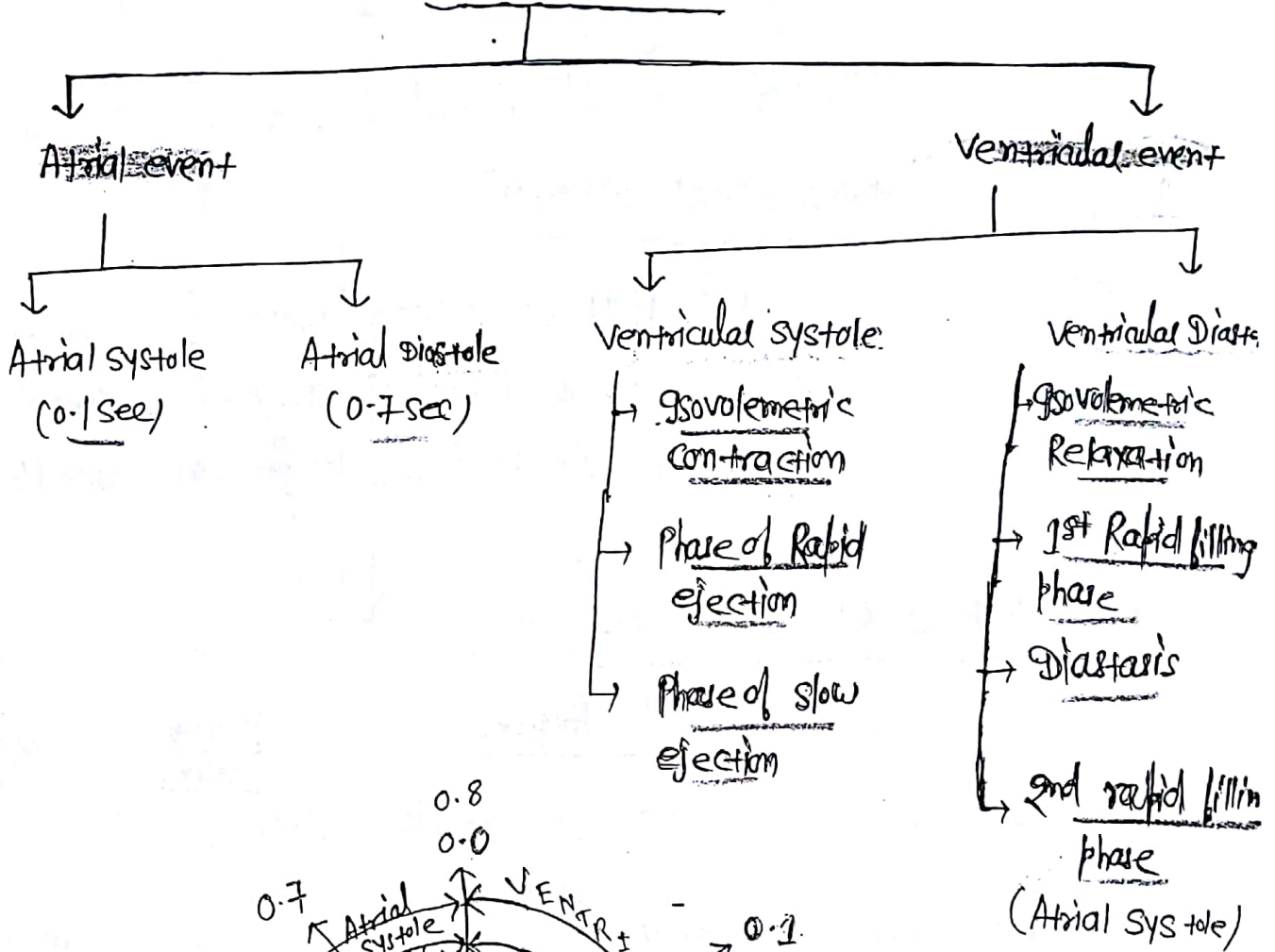
CARDIAC CYCLE **

(39)

* Electrical & Mechanical changes which occur in heart from one beat to Next.

* Cardiac cycle time = 0.8 sec

CARDIAC CYCLE 5.9



* ATRIAL PRESSURE (Atria \Rightarrow Low pressure zone)

Diastole \Rightarrow 0-3 mm Hg

Atria
 \hookrightarrow Primer pump

systole \rightarrow Right Atrial Pressure \Rightarrow 4-6 mm Hg

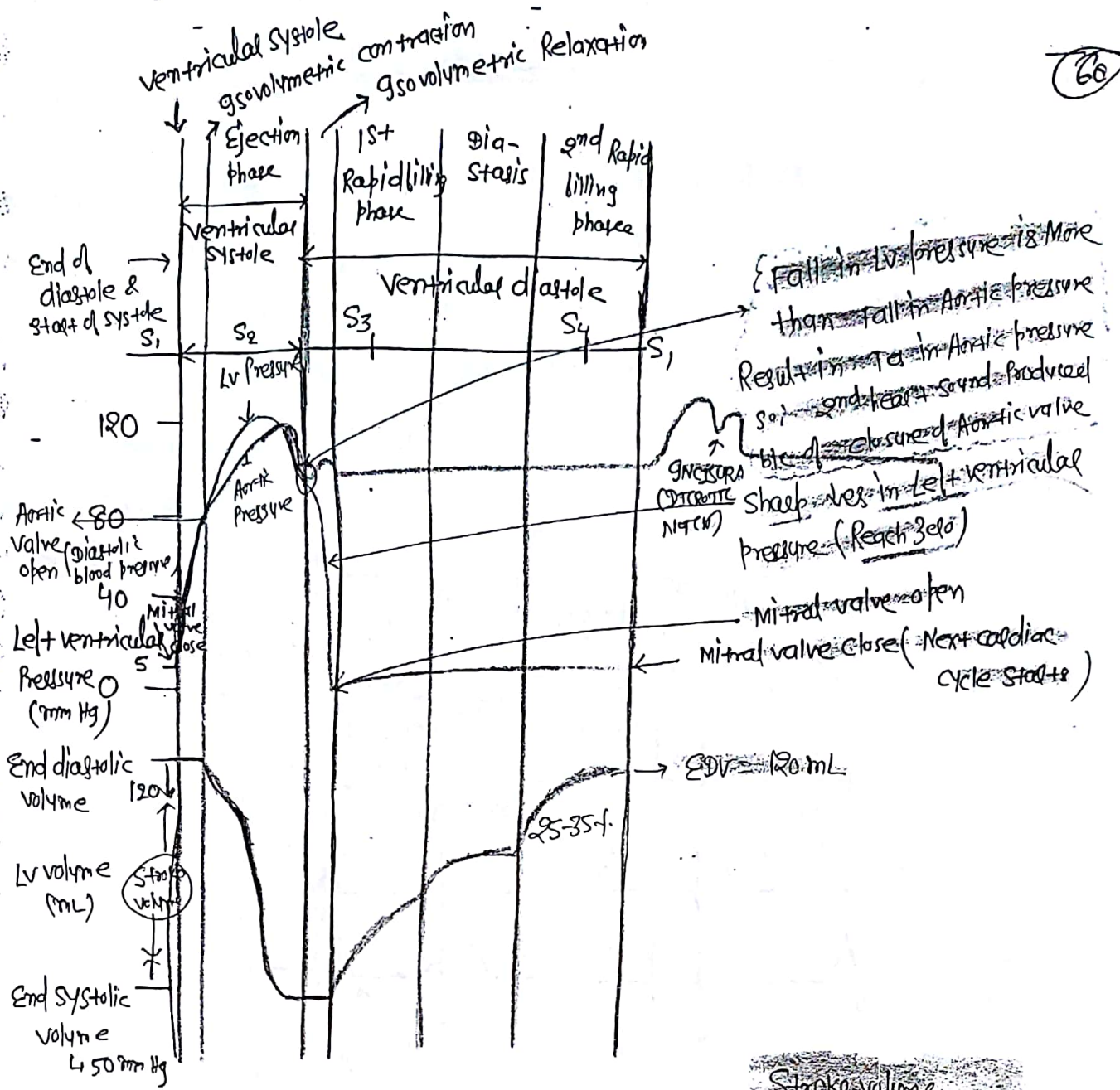
\rightarrow Left Atrial Pressure \Rightarrow 6-8 mm Hg

Pressure of Left Atrial Pressure is More d/t
" Physiological shunting "

\hookrightarrow Part of venous blood from coronary circulation & bronchial circulation directly into Left Atrium (so, it receives more blood)

* VENTRICULAR PRESSURE \rightarrow

	<u>Systolic Pressure</u>	<u>Diastolic Pressure</u>	<u>MAP</u>
<u>Left ventricle</u>	120 mm	0 (0-5 mm)	—
<u>Systemic circulation</u>	120 mm	80 mm	93 mm
<u>Right ventricle</u>	25 mm	0	
<u>Pulmonary circulation</u>	25 mm	0 (0-5 mm) 9 mm	15 mm



$S_1 \Rightarrow$ closure of Mitral valve

$S_2 \Rightarrow$ closure of Aortic valve

$S_3 \Rightarrow$ 1st Rapid filling Phase

\rightarrow May be present in children & Normal young adults

$\rightarrow \oplus$ In condition of left ventricular complication

\rightarrow as in Left ventricular hypertrophy; congestive cardiac failure.

$S_4 \Rightarrow$ 2nd Rapid filling phase

\rightarrow coincides with Atrial systole (Always pathological) Always pathological

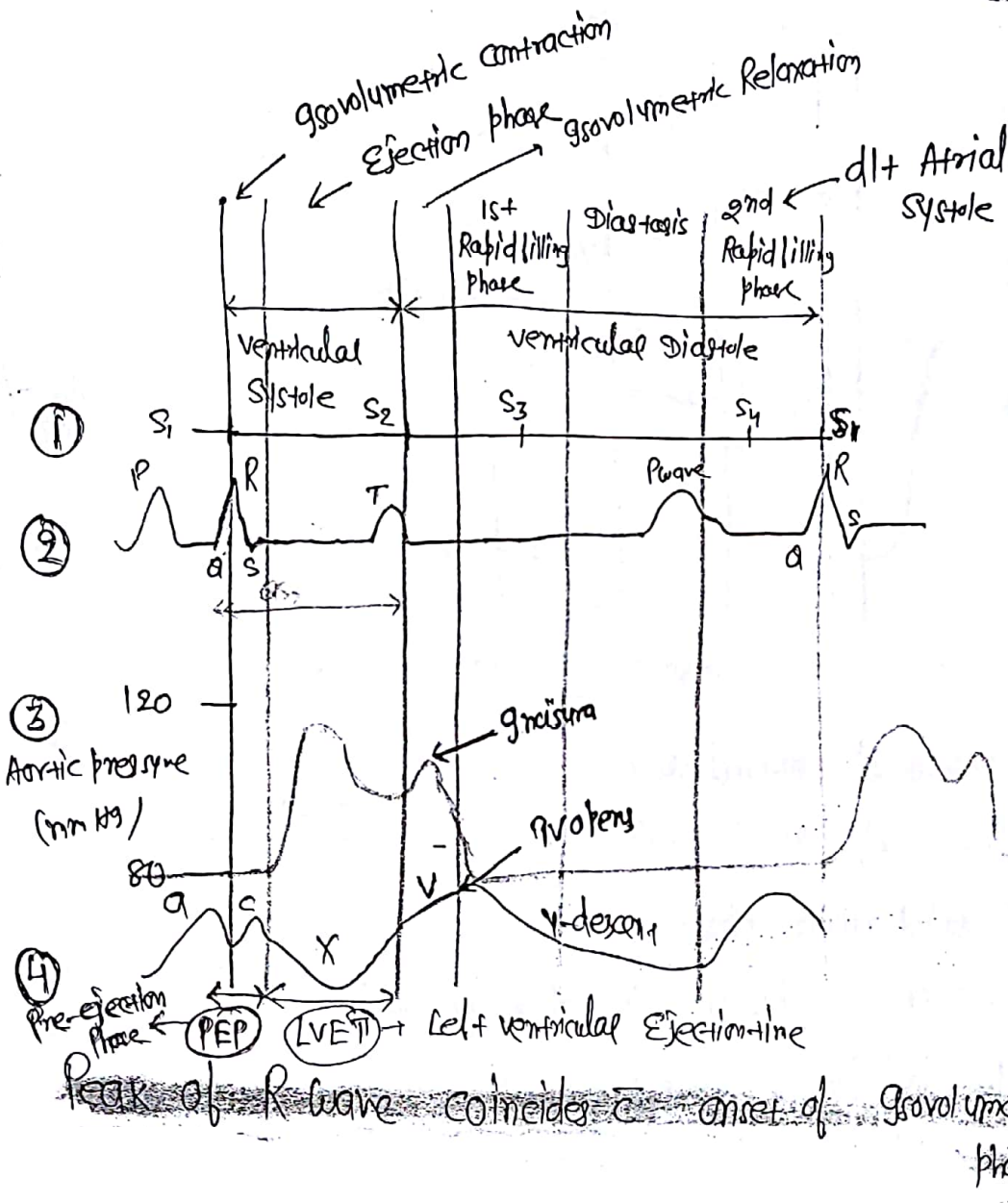
\rightarrow present in left ventricular compliance

INCISURA \Rightarrow It is towards the end of ventricular systole;

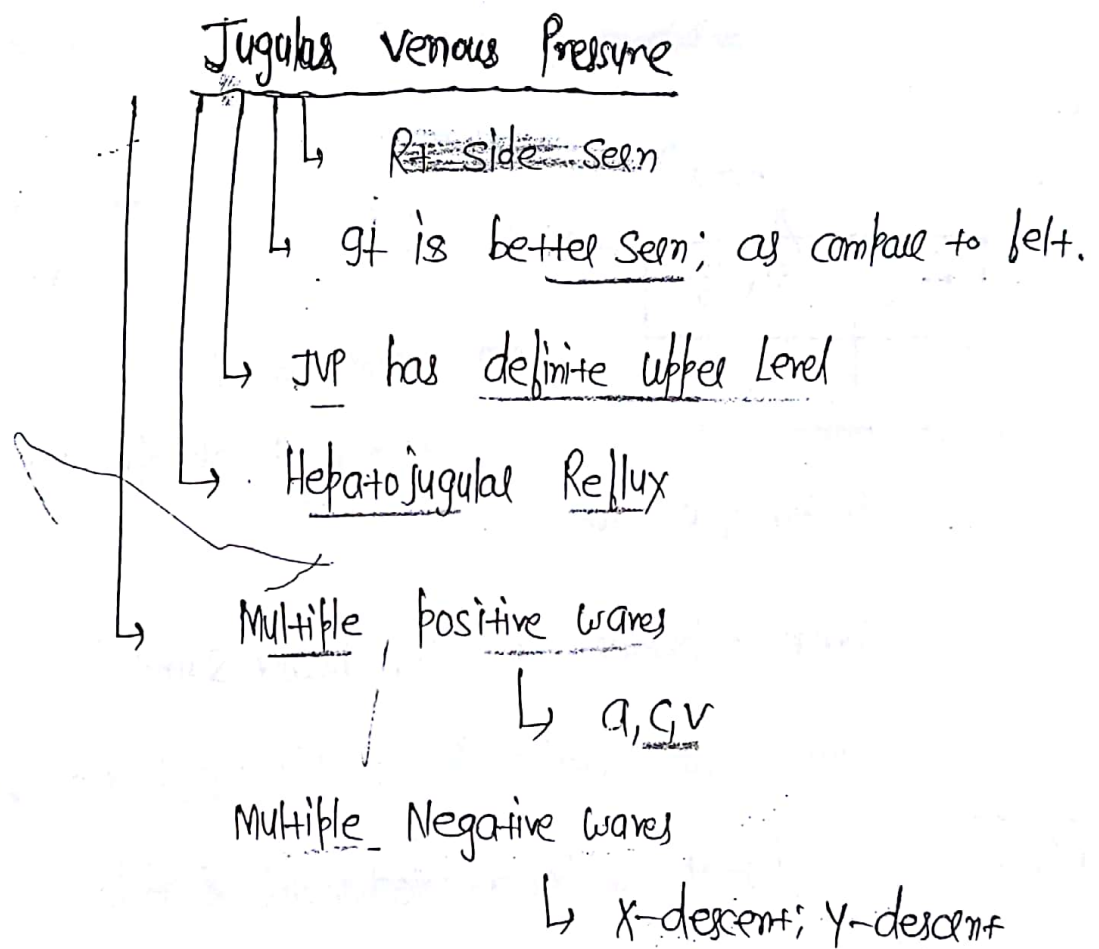
\hookrightarrow Left Ventricular pressure become lower than Aortic pressure;
 So; Aortic blood tends to flow back into Left ventricle;
 But this stream of Aortic blood hits the now close Aortic valve \rightarrow INCISURA ON AORTIC PRESSURE CURVE

aka "Dicrotic Notch"

\hookrightarrow coincides \bar{c} S₂ heart sounds



S ₁ heart sounds	<u>coincides</u> \bar{c} \rightarrow	Peak of " <u>R</u> " wave	(61)
S ₂ heart sounds	<u>"</u> \rightarrow	End of " <u>T</u> " wave	
S ₃ heart sounds	<u>"</u> \rightarrow	blw " <u>T</u> " & Next " <u>P</u> " wave	
S ₄ heart sounds	<u>"</u> \rightarrow	<u>PR Interval</u> .	



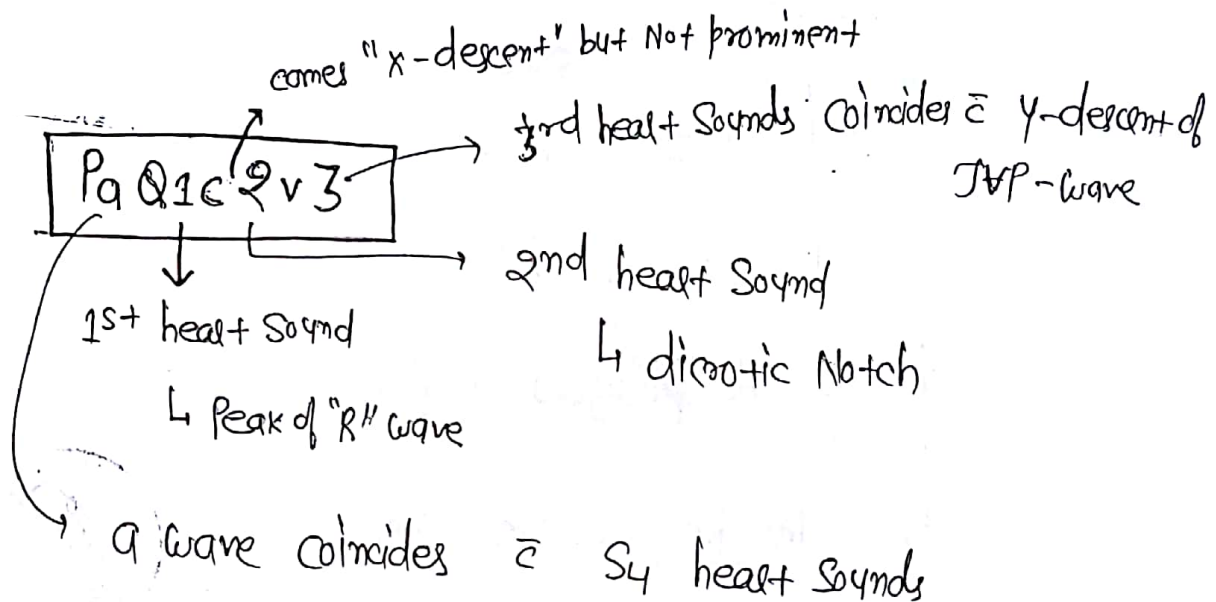
a-wave \Rightarrow Atrial systole

c-wave \Rightarrow Bulging of closed Tricuspid valve into Right Atrium during isovolumetric contraction phase

X-descent \Rightarrow Downward pull of closed Tricuspid valve during ejection phase

V-wave \Rightarrow d/t Venous filling of Right Atrium just before opening of Tricuspid valve

Y-descent \Rightarrow Flow of blood from Right Atrium into Right Ventricle after opening of Tricuspid valve



* If we Record heart sounds, ECG & Phonocardiogram Simultaneously \rightarrow

QS₂ \rightarrow Total Electro-Mechanical Systole

\hookrightarrow It is from onset of "Q" wave to the onset of "S" heart sound

\hookrightarrow It includes Ventricular contraction + Electrical contraction both (QRS complex)

Left Ventricular Ejection time (LVET) :

(62)

It is from the onset of carotid pressure rise to Diastolic Notch.

Pre-ejection Period (PEP) : It is

$$\frac{QS_2}{LVET} \quad * \quad QS_2 = LVET$$

$$\frac{PEP}{LVET} = 0.35 \quad * \quad \frac{PEP}{LVET} = 0.35$$

In conduction Abnormality

$$\frac{PEP}{LVET}$$

→ Yes (b/c PEP Prolong & LVET(N))

Q88 Cardiologist

ECG

Phonocardiogram

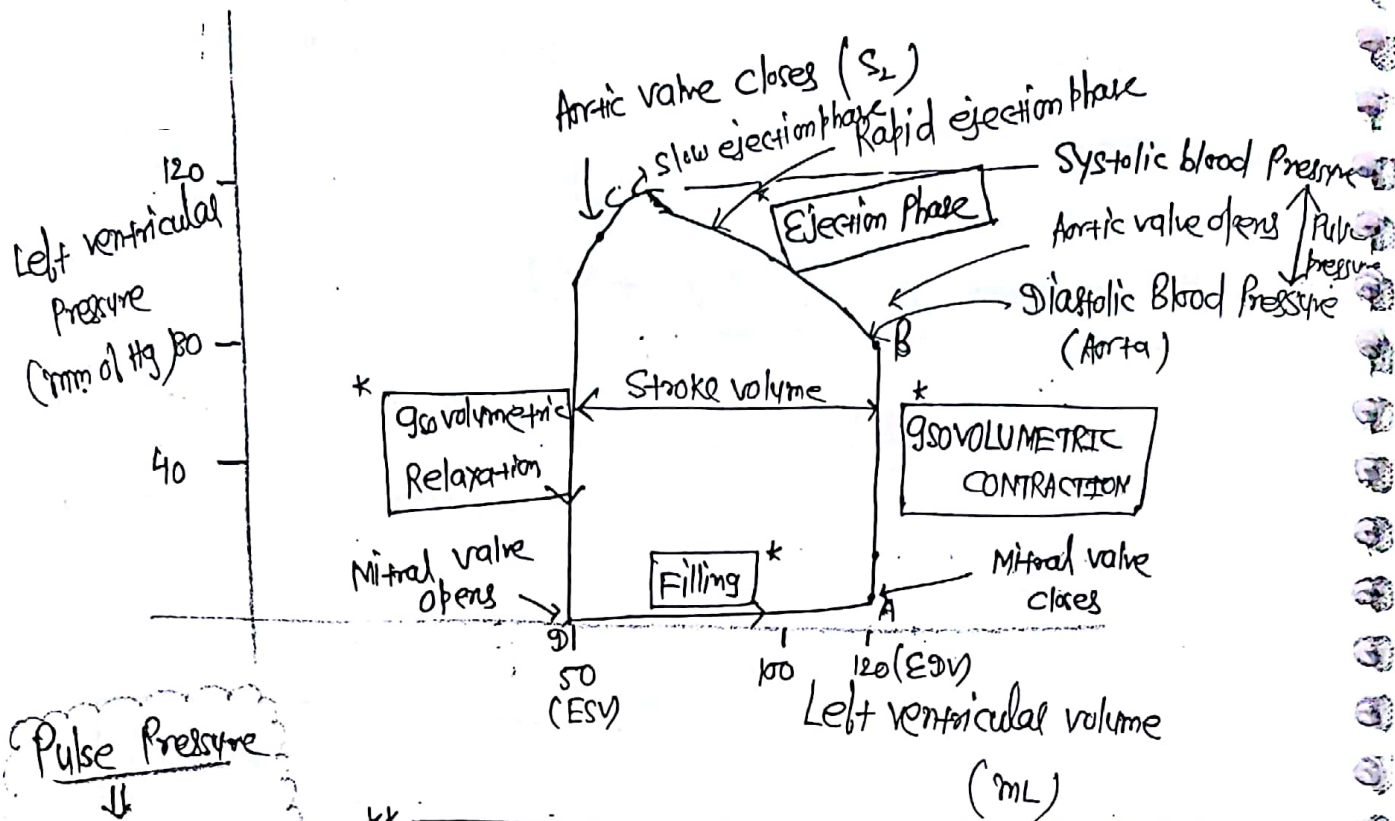
carotid pressure changes

} Recorded Simultaneously

his carotid pressure transducers Not functioning properly ??
Which of the following (N) ??

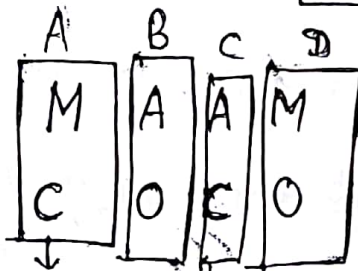
(A) ~~only QS₂~~ ; (B) QS₂ & LVET ; (C) LVET & PEP ; (D) All

LEFT-VENTRICULAR PRESSURE VOLUME LOOP

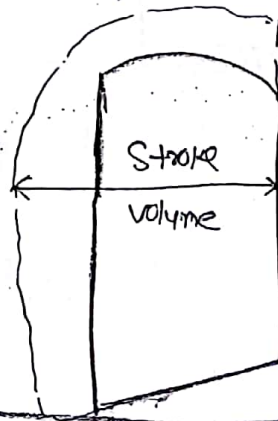


Pulse Pressure
 \downarrow
 SBP - DBP

$$\text{Ejection fraction} = \frac{\text{Stroke Volume}}{\text{End diastolic volume}}$$



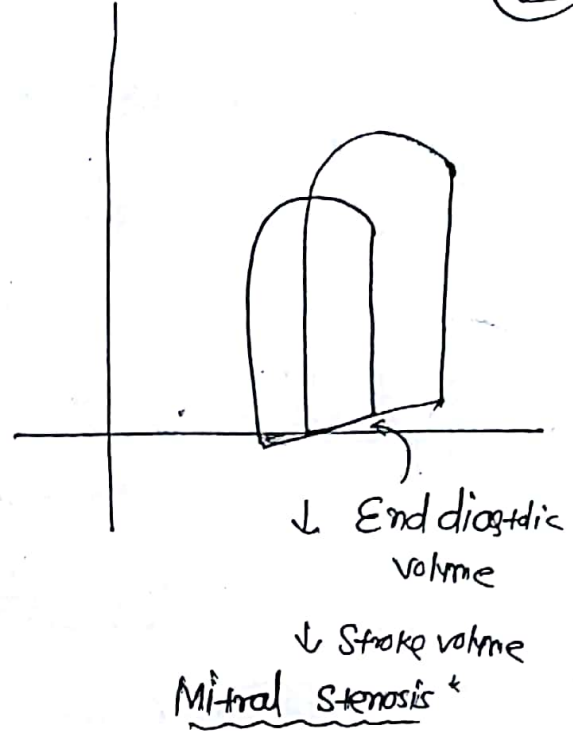
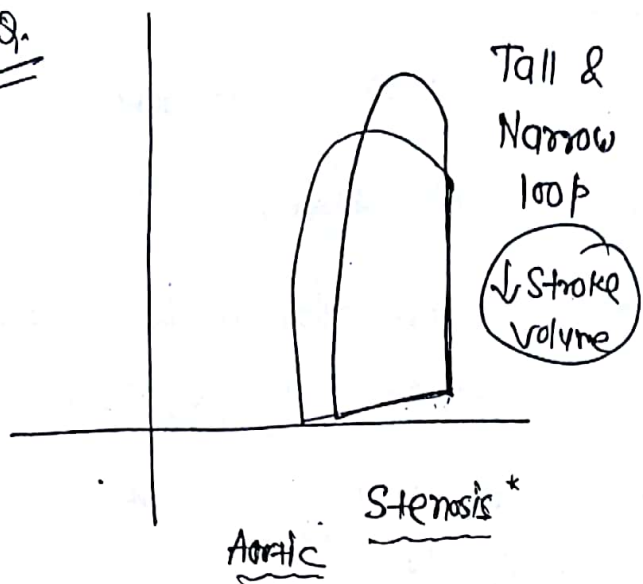
Qa
 Which Physiological
 condⁿ



Sympathetic Stimulation
of heart:

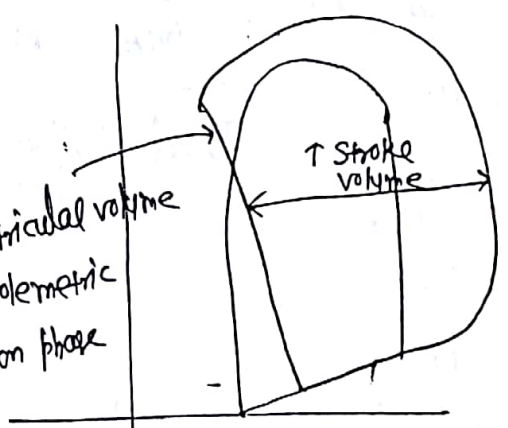
- ↑ Myocardial contractility
- ↑ Stroke volume
- ↑ Systemic Peripheral Resistance

QA



Left side shift of Loop

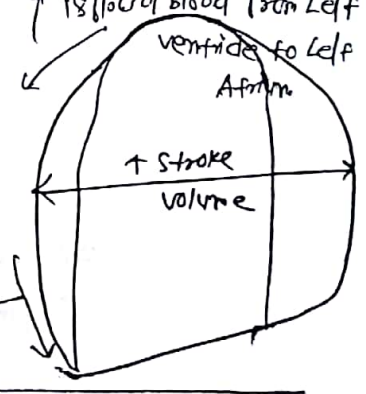
QA
↑ in Left ventricular volume in isovolumetric Relaxation phase



Look @ Isovolumetric Relaxation phase

higher systolic pressure*

↑ in Left ventricular volume b/c there is flow of blood from Left ventricle to Left Atrium



then ↑ in LV volume b/c LA pressure ↑ & cause ↑ in LV volume

Lower systolic pressure*



Right side shift of Loop

CARDIAC OUTPUT *

Volume of blood ejected per ventricle/minute

• Cardiac output = ~~5 Litres/min.~~

↳ it Means Left ventricular output is 5 Litres/min
& also Rt. ventricular output is 5 Litres/min

Left ventricular output is 1-2 L. More b/c of
"Physiological Shunting" *

Cardiac output = Left ventricular output = Systemic blood flow

cardiac output = Right ventricular output = Pulmonary blood flow

$$\rightarrow C.O. = \text{Systemic blood flow} = \frac{\overset{\text{Mean Atrial Pressure}}{\text{MAP}} - \text{Rt. Atrial Pressure (RAP)}}{\text{Total Peripheral Resistance (TPR)}}$$

$$\Rightarrow C.O. \Rightarrow \frac{\overset{100}{\text{MAP}} - \overset{0-3}{\text{RAP}}}{\text{TPR}}$$

$$\Rightarrow CO = \frac{MAP}{TPR} **$$

$$\Rightarrow MAP = CO \times TPR$$

(64)

$$\text{Cardiac output} = \frac{\text{Pulmonary Blood flow}}{5 \text{ L/min}} = \frac{\frac{150 \text{ mm}}{\text{Mean Pulmonary Pressure}} - \frac{8-12 \text{ mm}}{\text{PCWP}} - \cancel{\Delta \text{AP}}}{\text{Atrial Pressure (Left Atrial Pressure)}} \times \text{Pulmonary vascular Resistance}$$

⇒ Cardiac output = Heart Rate × Stroke volume

↑ Cardiac output ⇒ In Exercise (400-500 f. Tes)

Anxiety (200 f. Tes)

Excitement

Pregnancy

Standing to Lying Position (Venous Return)

Eating (30 f. Tes)

Hypertension

Beer - Beer

↓ Cardiac output ⇒ Lying to Standing Posture (Venous Return)

Hemorrhage

Hypothyroidism

Myocardial Infarction

* No change in cardiac output \rightarrow Sleeping

- Moderate change in Environment temperature

Regulation of cardiac output \rightarrow

Heart Rate

Stroke volume

\uparrow Heart Rate \Rightarrow \uparrow Cardiac output
(Sympathetic stimulation)

\uparrow Sympathetic

\uparrow Heart Rate

\uparrow Force of contraction

(When the heart rate \uparrow
 \downarrow
duration of all the phases \downarrow
 \hookrightarrow duration of diastole \downarrow
Much more than duration of systole)

Result in better emptying of ventricle

\uparrow stroke volume

(\downarrow End systolic volume)
Decrease end systolic volume

AIIMS May '18 **

\uparrow cardiac output

Increase cardiac output

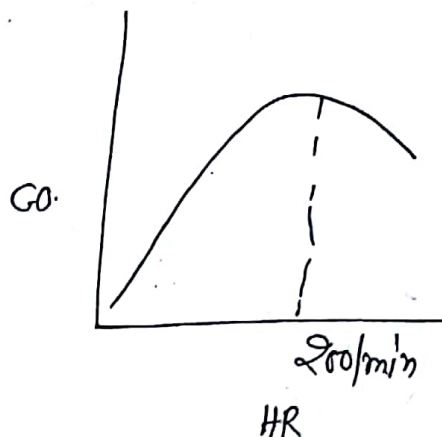
* When Heart Rate $> 180-200/\text{min}$

(65)

\Downarrow
 \Downarrow Diastolic Filling time

\Downarrow
 \Downarrow Stroke volume

\Downarrow
 \Downarrow Cardiac output



Stroke volume

Stroke volume

depends on

i) Myocardial contractility
Myocardial contractility

\uparrow Sympathetic
Inotropes
(Caffeine)

\uparrow contractility
 \uparrow Stroke volume
 \uparrow Cardiac output

ii) Venous Return
venous return

\uparrow Venous Return

\uparrow End diastolic
Volume (Preload)

\uparrow tension generated

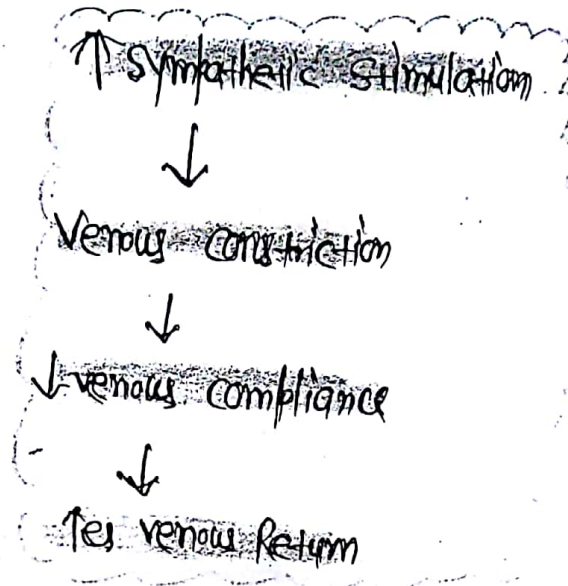
\uparrow Stroke volume

\uparrow Cardiac output

Frank-Starling Law, but
up to a physiological extent.

* Factors which affects venous Return :-

- i) Blood volume, (Tes \Rightarrow Venous Return Tes)
- ii) Sympathetic Stimulation;



iii) POSTURE :-

Lying \rightarrow Standing (Tes Peripheral Pooling)
↓ venous Return)

Standing \rightarrow Lying (Tes Venous Return)

iv) Calf Muscle Contraction

↳ Exercise \rightarrow ↑ Contraction \Rightarrow ↑ venous Return
Klas "Muscle Pump"

v) Deep Inspiration
↳ ↓ Pleural Pressure \rightarrow ↓ venous Return

*

Regulation of C.O.

(66)

Homometric regulation

HOMOMETRIC REGULATION

Includes factors which reg cardiac output and are independent of ventricular muscle fiber length.

- It includes all factors which affect:

a) Heart Rate*

b) Myocardial contractility*

HETEROMETRIC REGULATION

Includes factors which affect venous return & ventricular muscle fiber



*

VASCULAR FUNCTION CURVES

I. VENOUS RETURN CURVE →

Venous Return \Rightarrow Mean systemic filling pressure (P_{sf}) - Right Atrial Pressure (RAP)

5 L/min

P_1 P_2

Resistance to venous return

Mean systemic filling pressure (P_{sf}) \Rightarrow When heart stops beating or circulation comes to stand still, pressure in all vessels (Arterial & veins) Equilibrates \Rightarrow This pressure is 1/3rd "Mean systemic filling pressure"

- It Represents Distending pressure in circulation
@ a particular blood volume & vascular tone

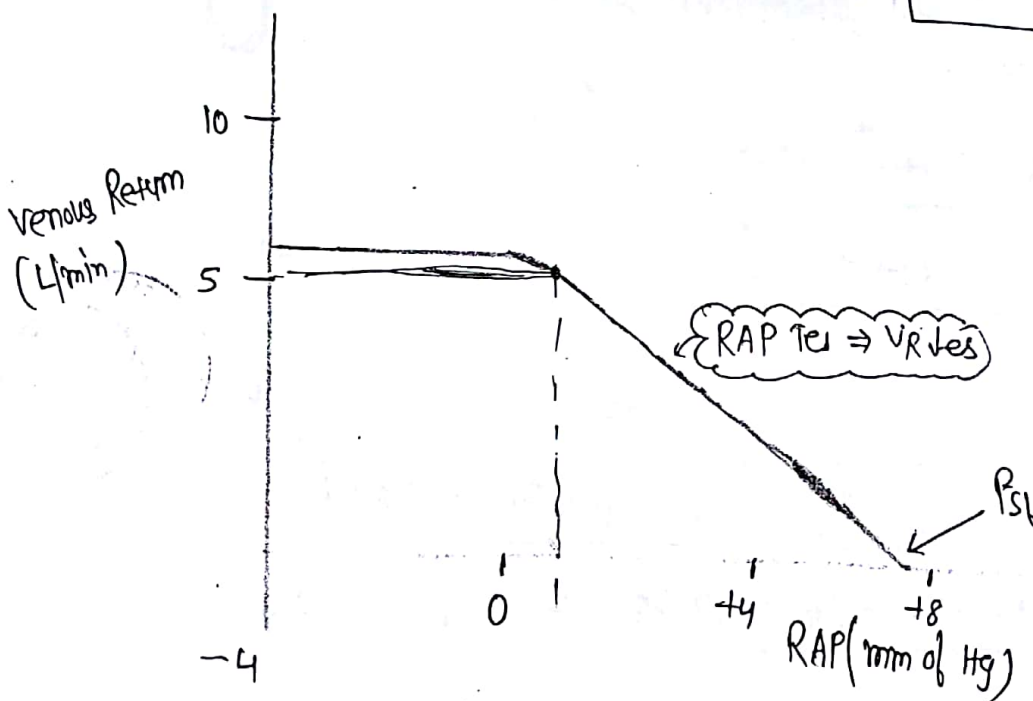
Blood volume and vascular tone

- 2 determinants

↳ Blood volume

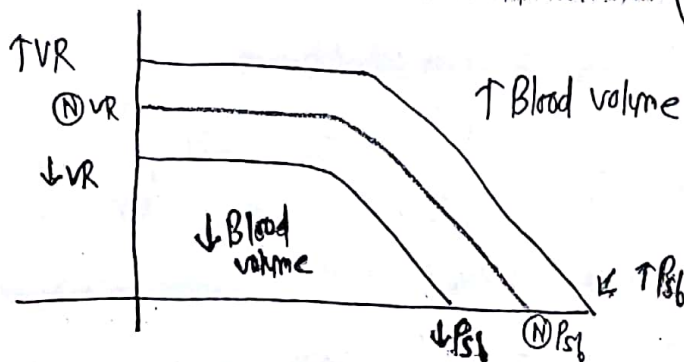
Venous tone.

$$V_R = \frac{P_{sl} - RAP}{\text{Resist. } V_R}$$

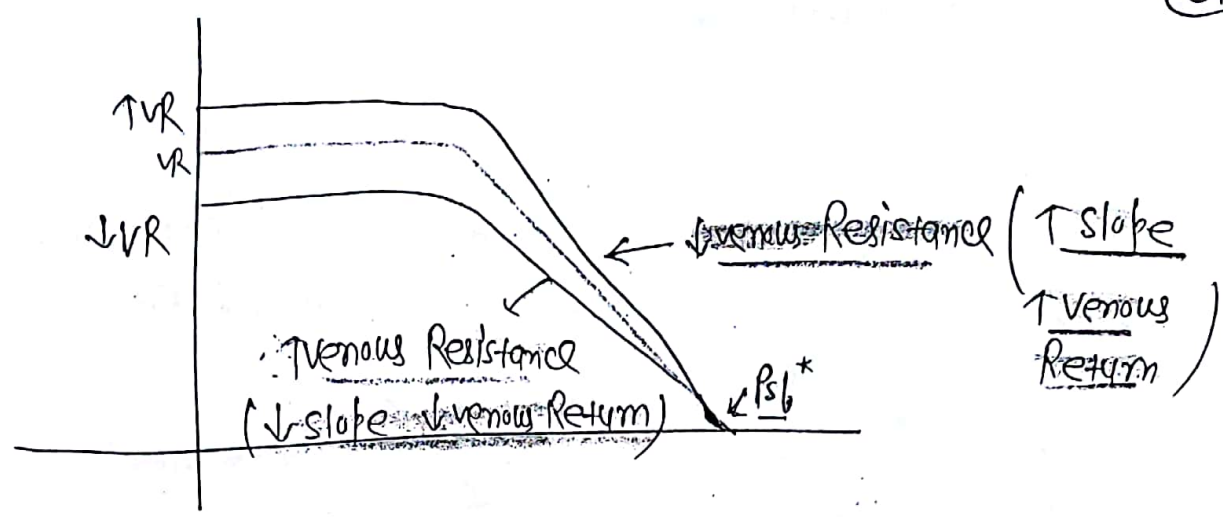


At Right Atrial Pressure (RAP) < 0 mm Hg ⇒ No further
res. in venous return (b/c vein tends to collapse)

QA.

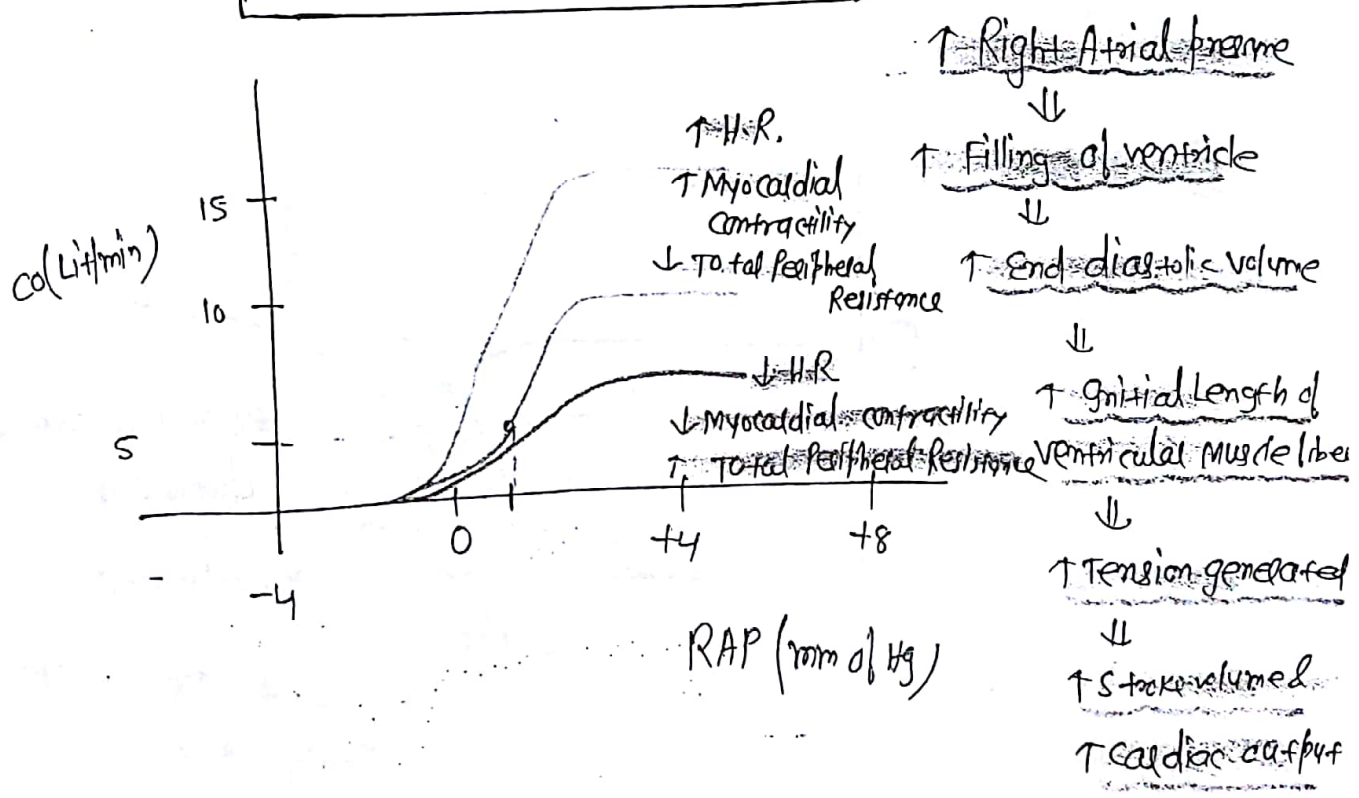


Q_Q

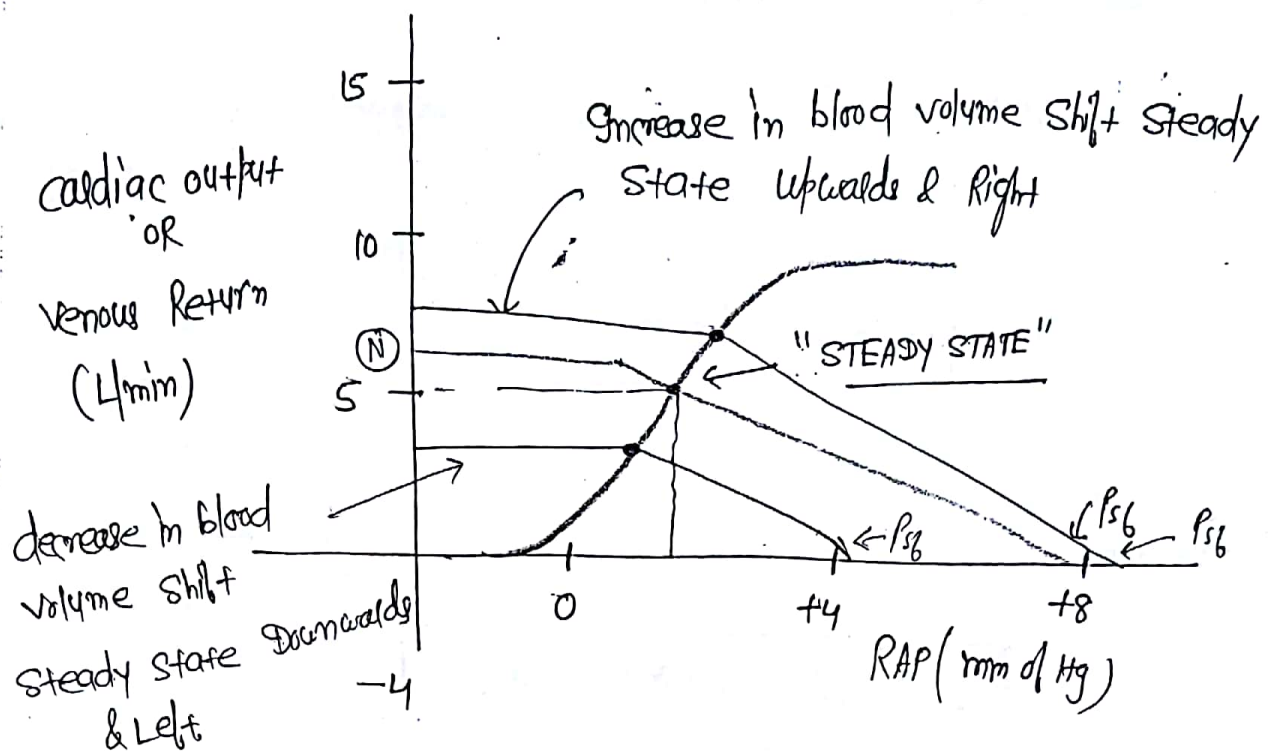


II.

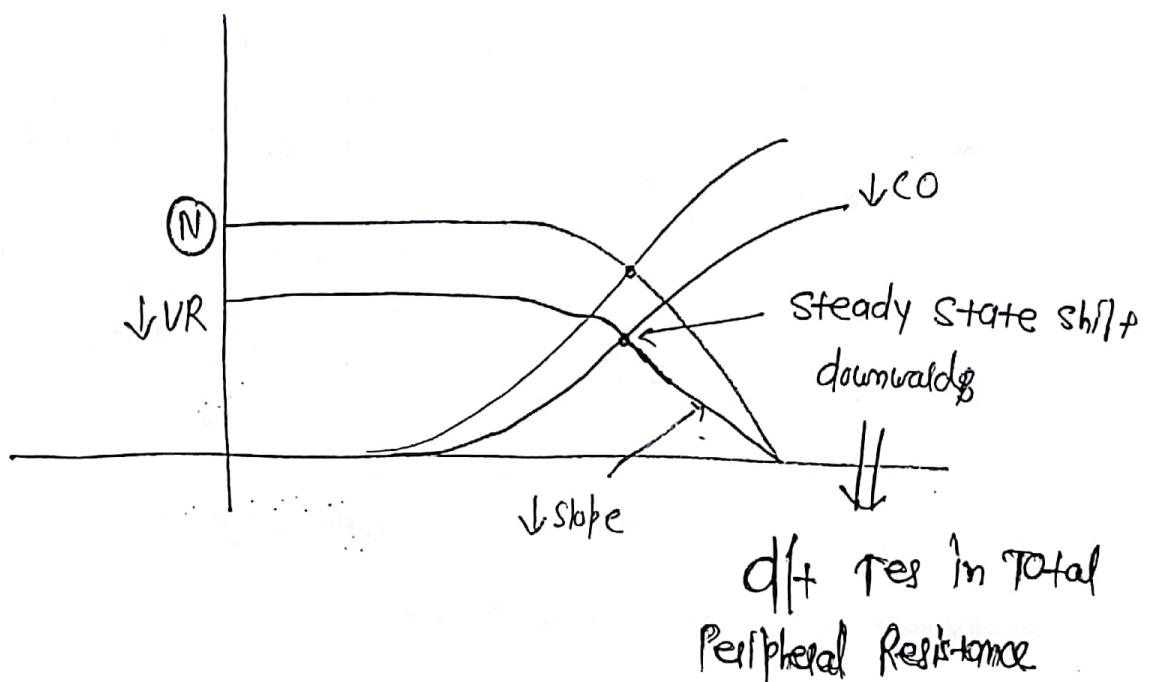
CARDIAC OUTPUT CURVES

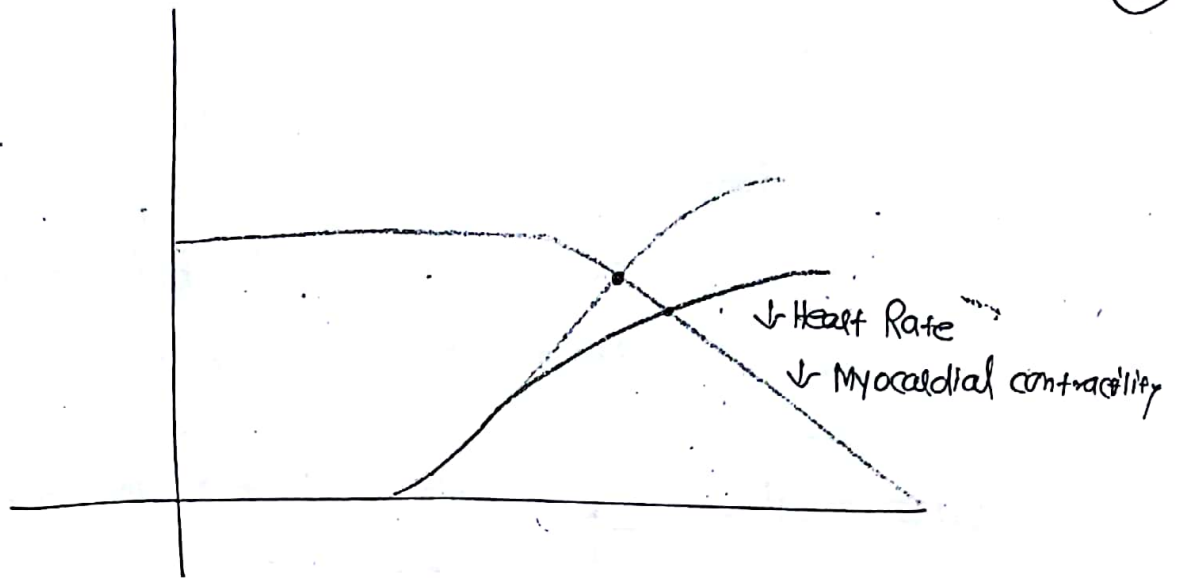
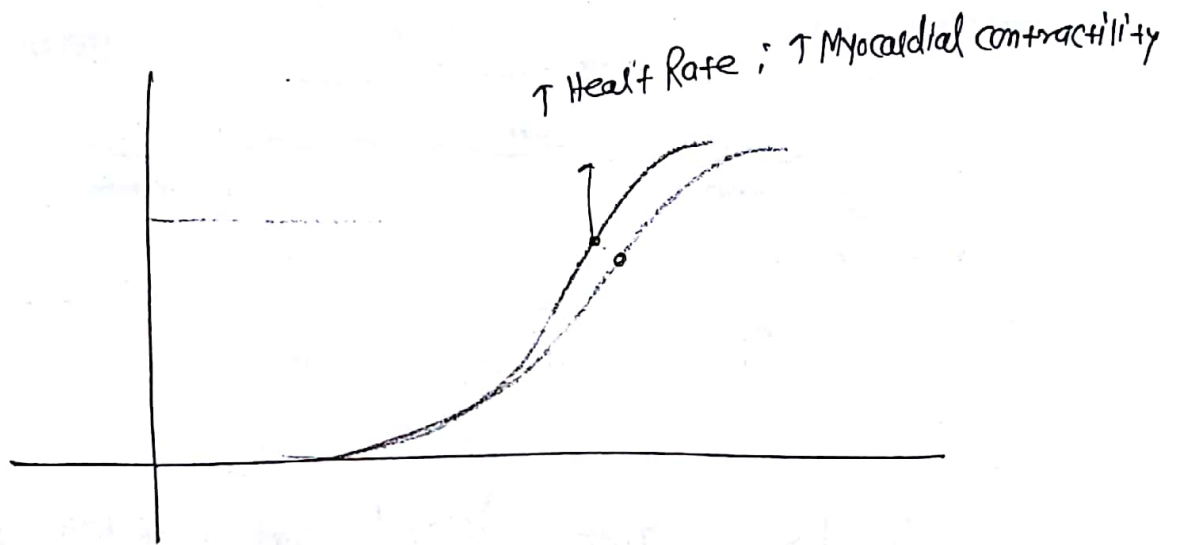


Steady state →



Q9.



QaQaQa

MEASUREMENT OF CARDIAC OUTPUT

(I) - NON-INVASIVE

↳ Echocardiography & Doppler Studies

(II)

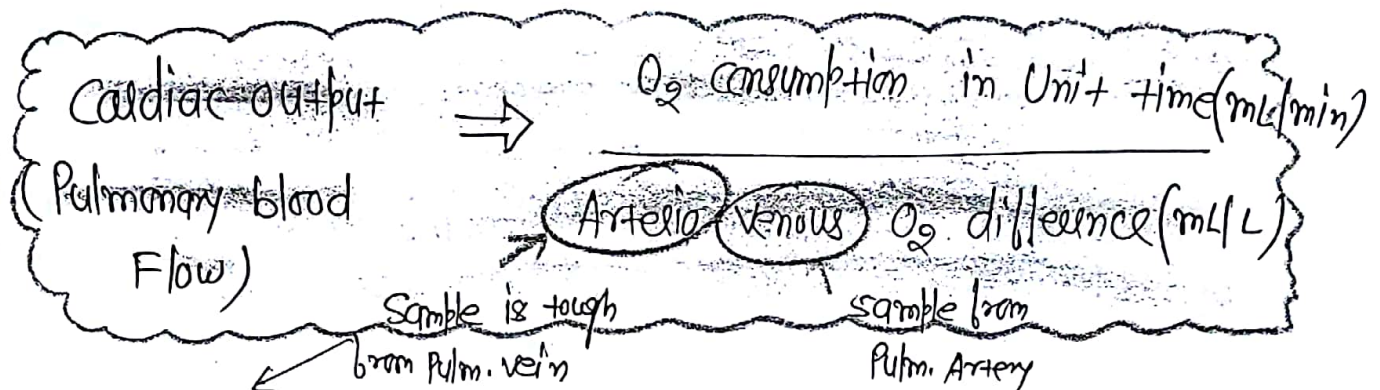
INVASIVE

↳ Fick's principle

Dye dilution technique

Thermodilution technique

FICK'S PRINCIPLE - Amount of a substance taken up by organ/whole body in unit time is equal to the product of blood flow through organ/whole body in unit time & Arterio-venous difference of that substance.



So; taken up by any Systemic Artery

$$= \frac{250 \text{ mL/min}}{190 \text{ mL/L} - 140 \text{ mL/L}} = \frac{250}{50} = 5 \text{ L/min}$$

Q In Fick's principle; Arterial Sample is taken from

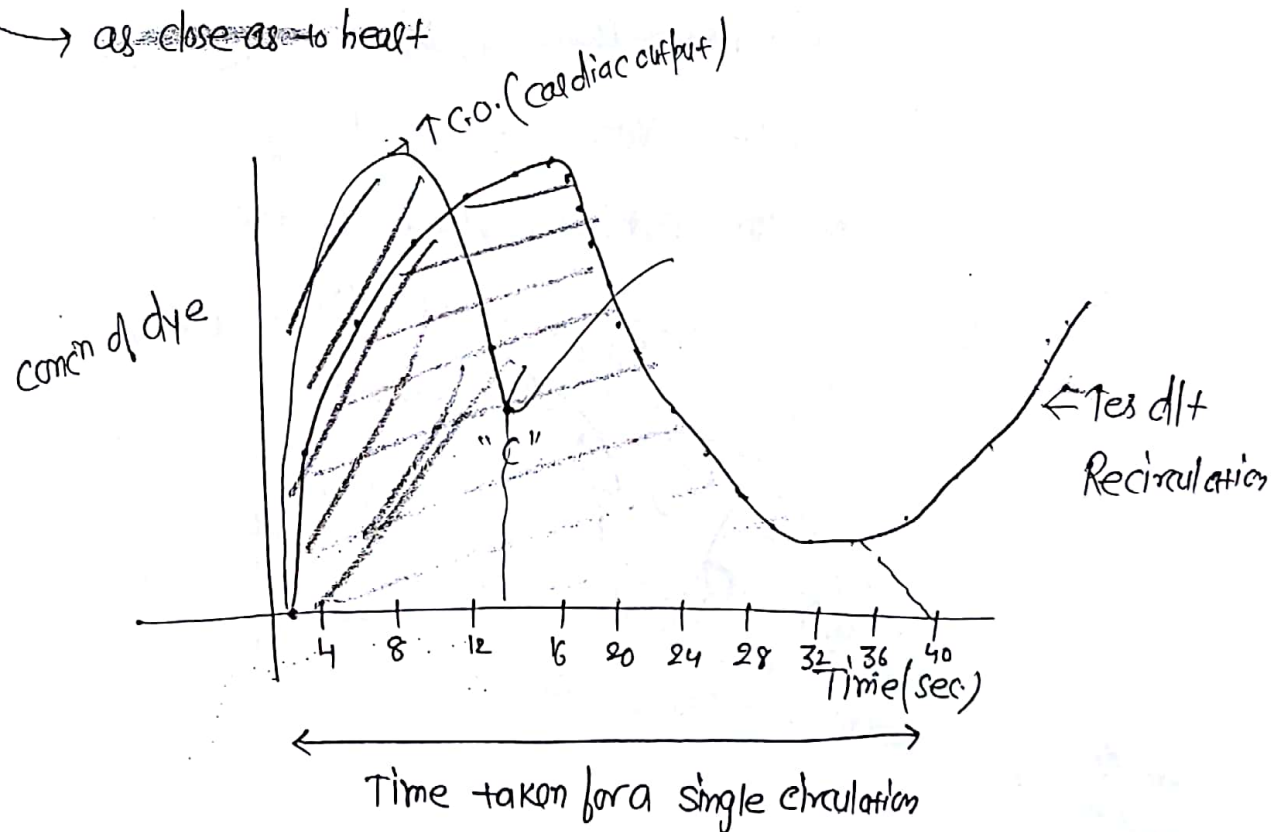
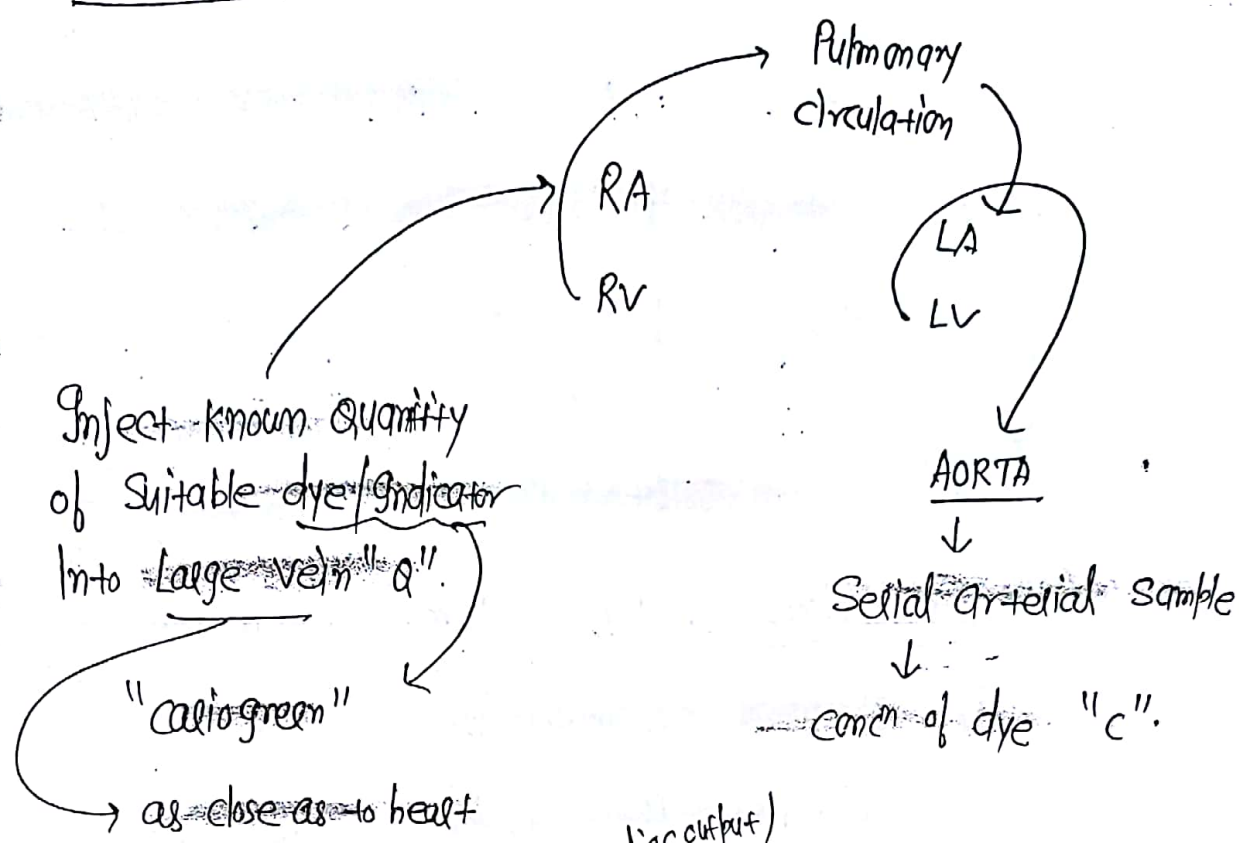
↳ Any Systemic Artery

Q Q

O ₂ consumption	600 mL/min
Arterial O ₂	24 mL/mL of blood
Pulm. A O ₂	18 mL/mL of blood

$$\text{Cardiac output} = \frac{600 \text{ (mL/min)}}{240 \text{ mL/L} - 180 \text{ mL/L}} = \frac{600}{60} = 10 \text{ L/min}$$

DYE - DILUTION TECHNIQUE



$$\text{Flow} = \frac{Q}{Ct}$$

$$\text{Flow} = \frac{Q}{Ct}$$

$$C = \text{concn of dye}$$

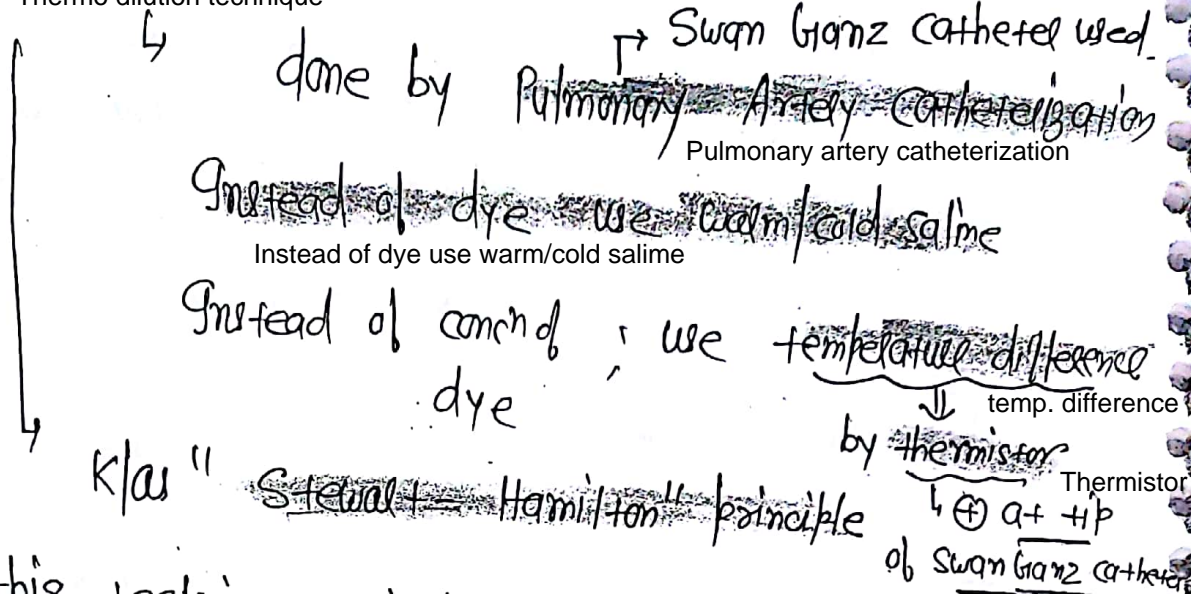
$$Q = \text{Volume of injected dye}$$

if 'c' is less = More cardiac output

(N) time = 39 sec

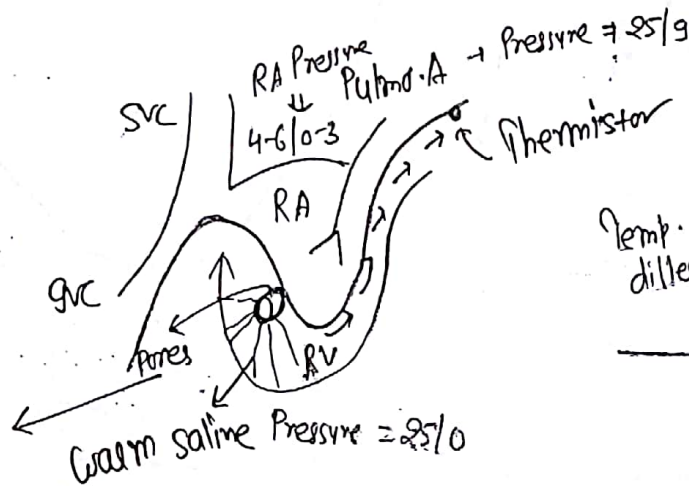
THERMODILUTION TECHNIQUE \Rightarrow done in gcu settings *

Thermo dilution technique

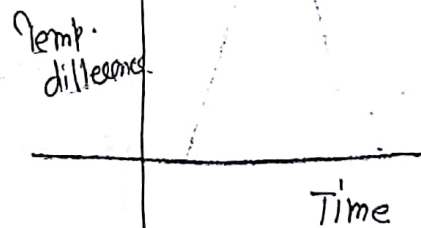


* this technique will be Unreliable in conditions of \rightarrow

- ① Tricuspid Regurgitation
- ② Pulmonary Regurgitation
- ③ Large Ventricular Septal defect
- ④ Very Low cardiac output.



through it introduces the warm saline



BLOOD PRESSURE

SBP \Rightarrow Max^m pressure during systole

DBP \Rightarrow Min^m pressure during diastole

Pulse pressure \Rightarrow S.B.P - D.B.P.

MAP \Rightarrow D.B.P + $\frac{1}{3}$ P.P (Pulse pressure)

QA Best Indicator of TPR \Rightarrow

① DBP

② MAP

2 determinants of Pulse pressure \Rightarrow

a) Stroke volume \Rightarrow \uparrow SV \uparrow P.P. (AR)
 \downarrow S.V. \downarrow P.P. (AS)

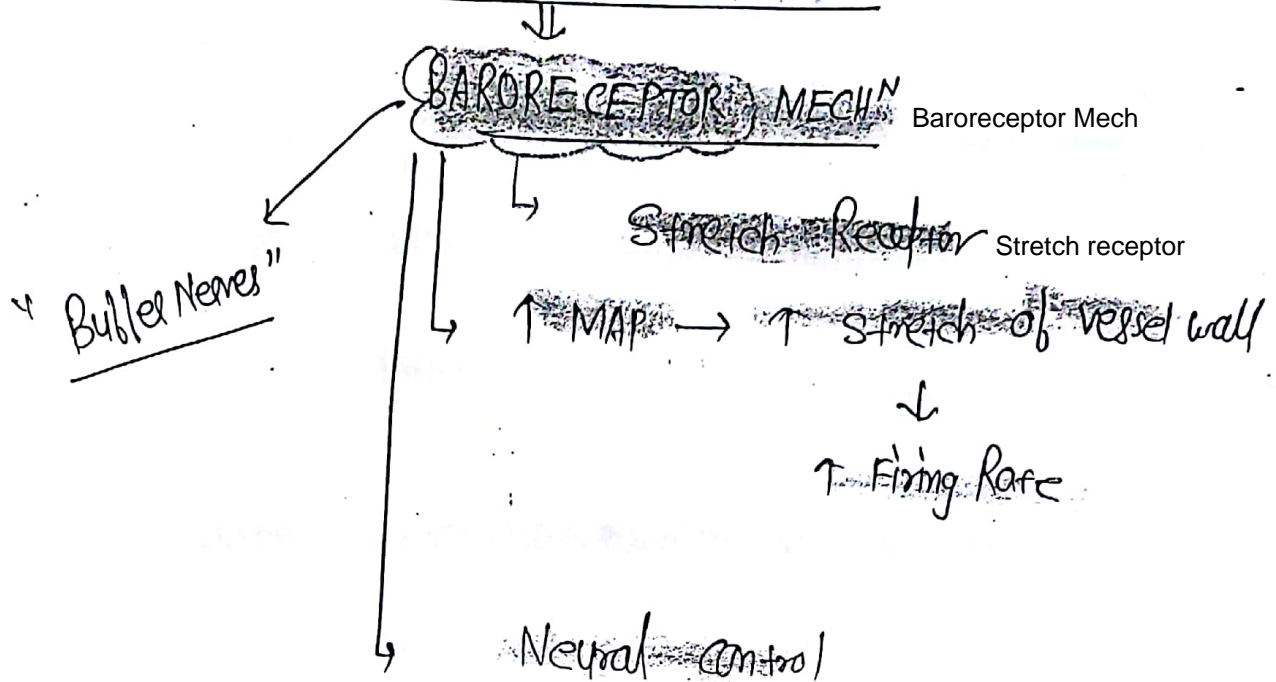
b) Arterial compliance (A.C) \Rightarrow \uparrow A.C \downarrow P.P.

Sclerosis \Rightarrow \downarrow A.C \uparrow P.P.
Sclerosis

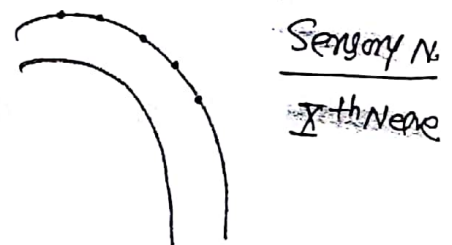
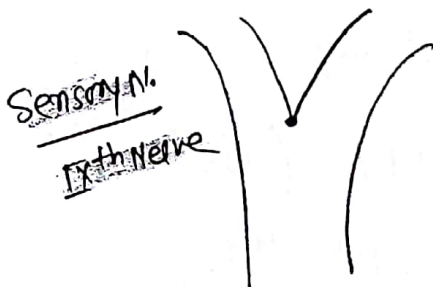
QA Ratio of Stroke volume & Arterial compliance approx determine \Rightarrow

$$\text{PP} \propto \frac{\text{SV}}{\text{ART compliance}}$$

REGULATION OF B.P.



- Response → Immediate
- Adaptation ⊕
- Imp. for Short-term Regulation (Min. - to - Min. Regulation)



Carotid Sinus Baroreceptor

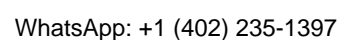
Aortic Arch Baroreceptor

→ 5th time more sensitive than Aortic Arch Baroreceptor

Threshold for Activation of Baroreceptor

↳ MAP of 50 mm Hg

K/a "CARDIO -
INHIBITORY
AREA"



$\uparrow \text{MAP} \rightarrow \uparrow \text{Stretch} \rightarrow \uparrow \text{Firing Rate}$ $\begin{matrix} \downarrow \text{Sympathetic} \\ \uparrow \text{Parasympathetic} \end{matrix}$

dual Role by

Sympathetic & Parasympathetic stimulation

$\downarrow \text{Heart Rate}$

$\downarrow \text{B.P.}$

$\downarrow \text{MAP} \rightarrow \downarrow \text{Stretch} \rightarrow \downarrow \text{Firing Rate}$ $\begin{matrix} \uparrow \text{Sympathetic} \\ \downarrow \text{Parasympathetic} \end{matrix}$

$\uparrow \text{Heart Rate}$

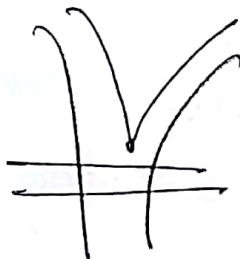
$\uparrow \text{B.P.}$

Q.Q. Carotid Sinus Stimulation \rightarrow

(A) $\uparrow \text{B.P.}$ $\uparrow \text{HR}$

~~(B)~~ $\downarrow \text{B.P.}$ $\downarrow \text{HR}$ (Moderate)

Q.Q. B/L clamping of carotid Arteries below carotid sinus



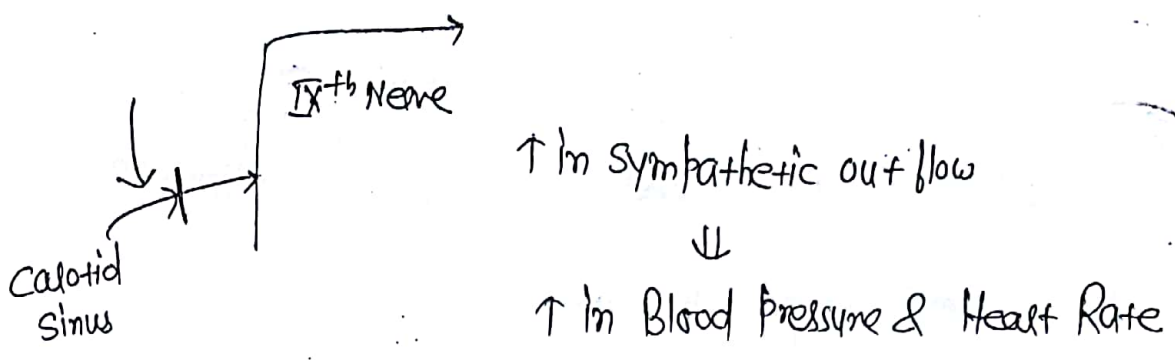
Moderate Tes In B.P. & T HR

Q.Q. B/L clamping of carotid Arteries @ carotid sinus

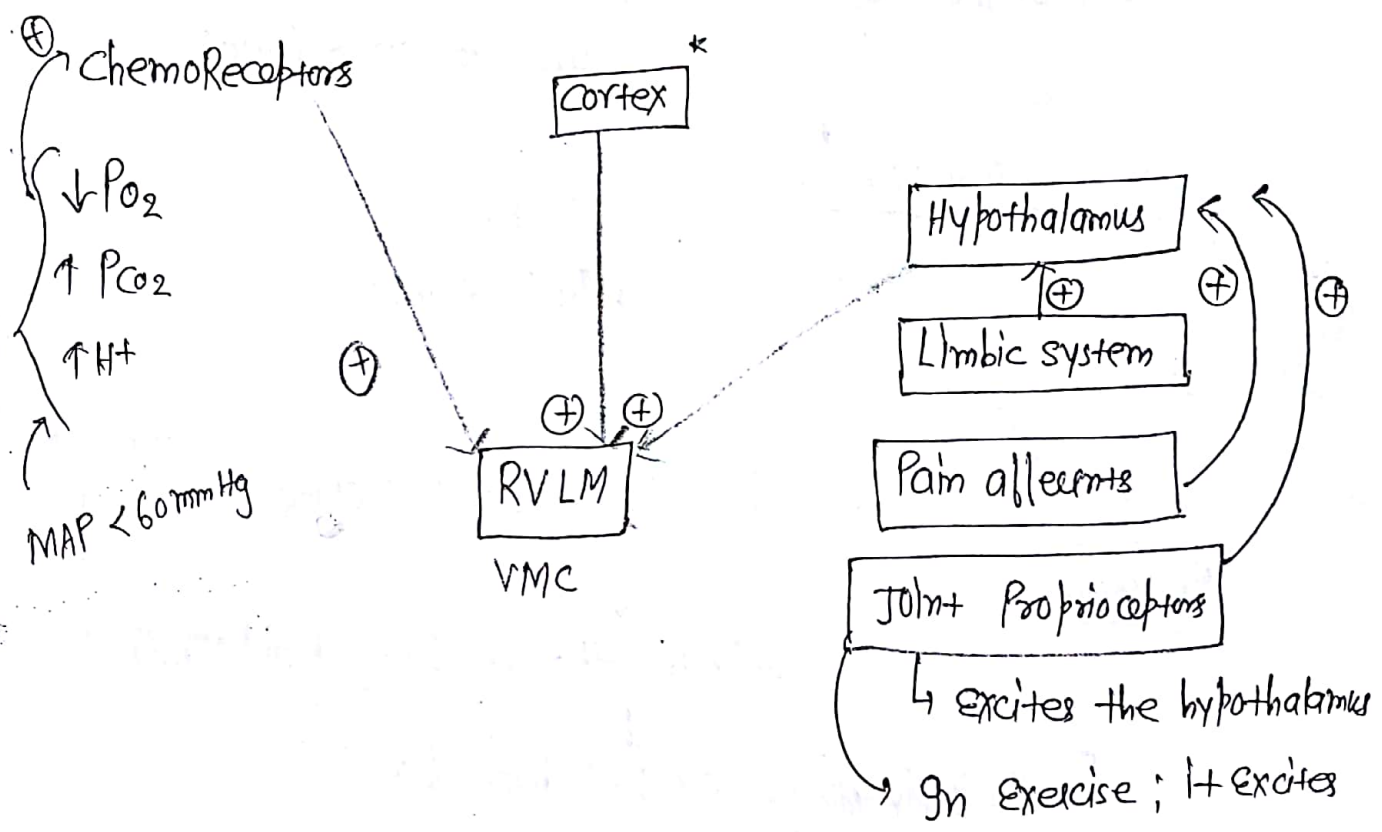


$\downarrow \text{B.P.}$ & $\downarrow \text{HR}$

Q. Q. B/L Section of HERING's Nerve (Carotid Sinus Nerve)



OTHER INFLUENCES ON VASOMOTOR CENTER [RVLM] →



CNS ISCHEMIC RESPONSE

- ~~Seen~~^{gn} b/w MAP of 65 & 140 mm of Hg

↳ cerebral blood flow is constant
(b/c of Autoregulation)



but if MAP < 65 mm of Hg \Rightarrow ↓ cerebral blood flow



CNS Ischemia



direct & very strong stimulation of
Vaso Motor Centre (VMC)



↑↑ BP

↑↑ HR

* Most powerfully activated

① MAP of 40 mm of Hg



Klas "LAST DITCH STAND"

* CUSHING'S
RESPONSE



↑↑ Intracranial Pressure



Compress the cerebral blood vessels



↓ cerebral blood flow



CNS Ischemia

↳ CNS Ischemic Response

Direct & very strong stimulation of VMC

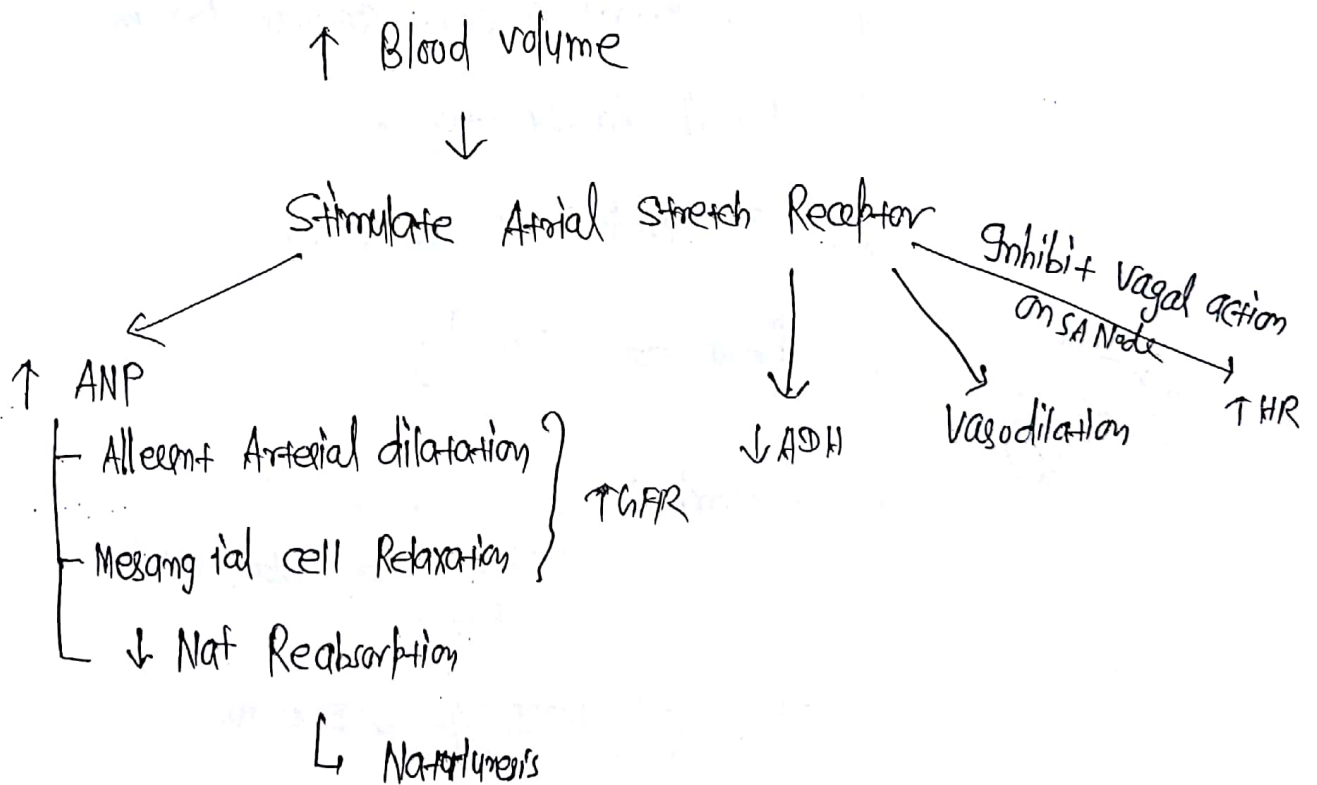
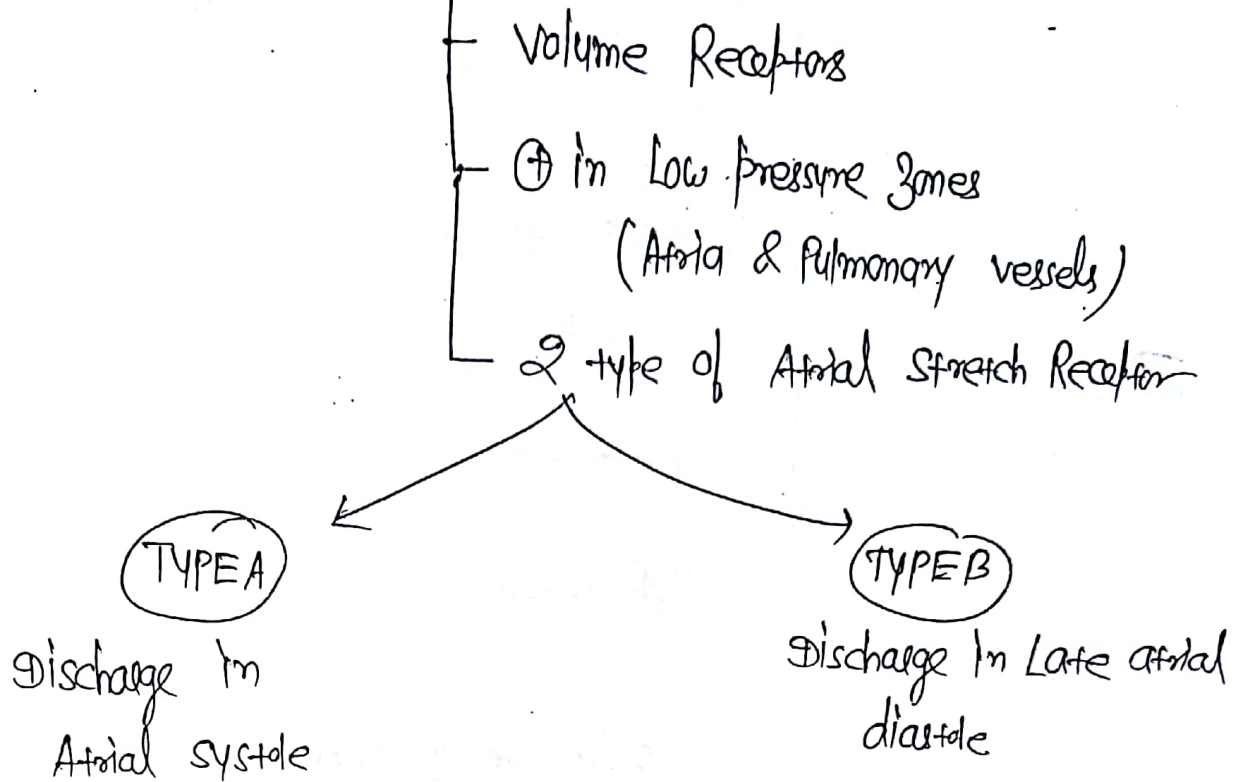
↑
Intact baroreceptor
Mechⁿ

↑↑ BP



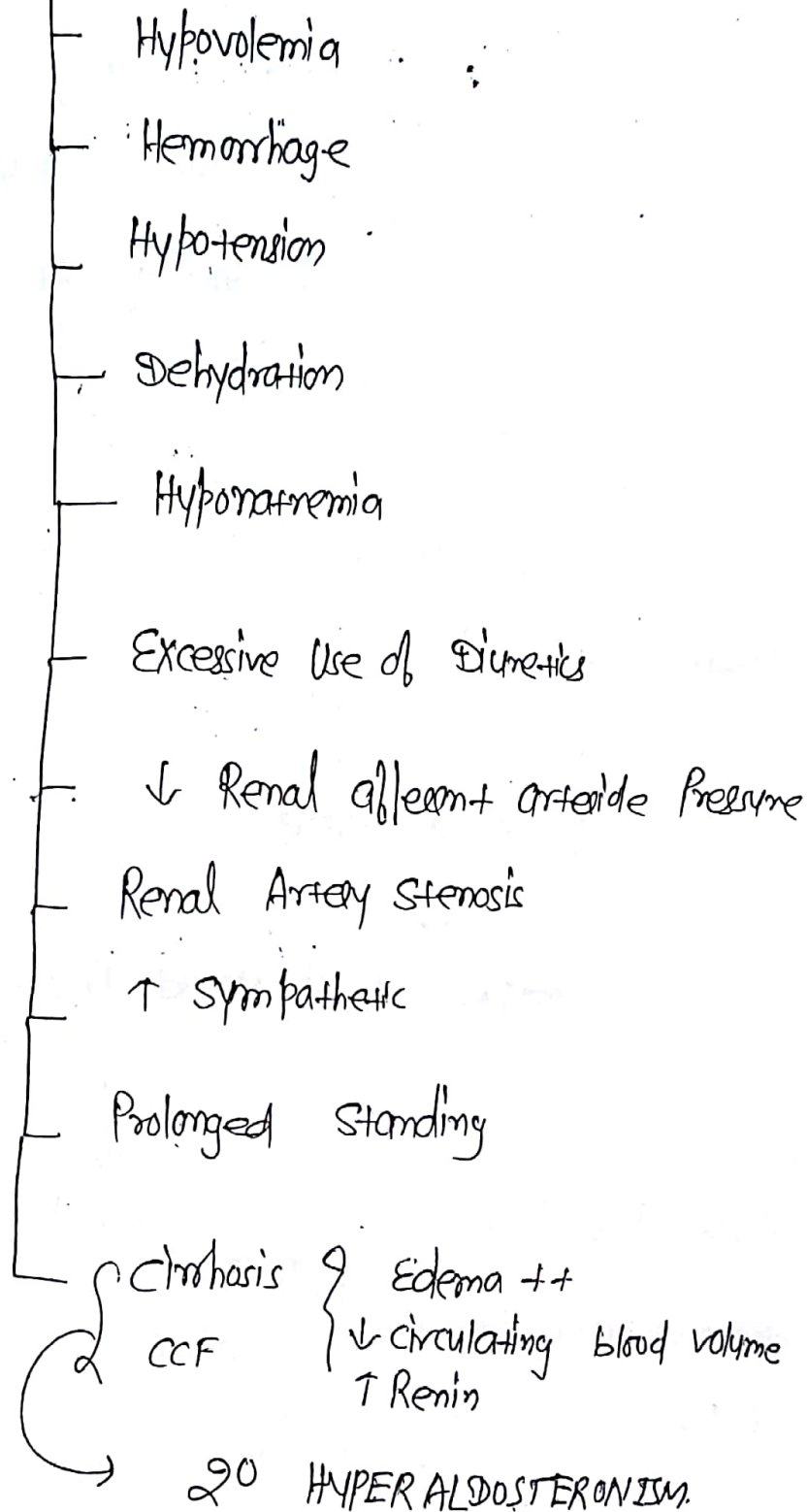
ATRIAL STRETCH RECEPTOR RESPONSE

93

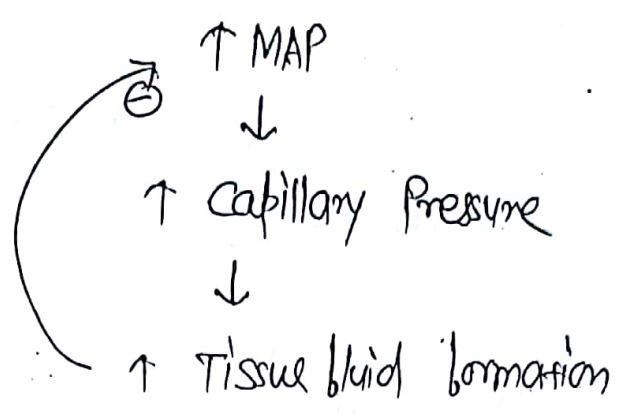


RAAS

Stimuli which ↑ Renin (JG cells) ⇒



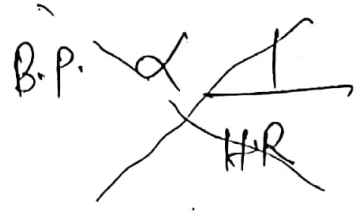
* CAPILLARY FLUID SHIFT \Rightarrow



MARRY'S LAW

Heart Rate $\propto \frac{1}{\text{blood Pressure}}$

Physiological basis
 \downarrow
Baroreceptor Response



BAINBRIDGE REFLEX

Sudden \uparrow in blood volume \rightarrow \uparrow Heart Rate
i) \downarrow Atrial stretch \uparrow Receptor pressure
in direct stretch of SA node

BEZOLD-JARISH REFLEX (CORONARY CHEMOREFLEX)

- Injection of -
Serotonin 99
capsaicin
Veratridine
Phenylguanides

} Into Carotid Arteries



Causes Apnea followed by Rapid shallow ventilation



Hypotension
Bradycardia

75

RENAL PHYSIOLOGY

(77)

Excretion \Rightarrow Filtration - Reabsorption + Secretion

Glomerular Filtration Membrane \Rightarrow

(i) Glomerular capillary Endothelium

- \rightarrow Fenestrated
- \rightarrow Large pores \oplus
- \rightarrow 70-80 nm

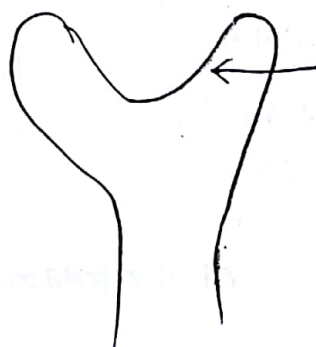
(ii) Basement Membrane (Limiting factor for filtration)

- \rightarrow No Pores
- \rightarrow Permeability is equivalent to pore size of 8 nm
- \rightarrow Proteoglycans / Sialoproteins \oplus



Gives \ominus ve charge to basement Membrane

iii)



visceral Layer of Bowman's capsule

\downarrow
Modified to form Podocytes

Filtration slits \oplus

\hookrightarrow 25-30 nm

* Neutral Substance $> 8\text{nm} \Rightarrow$ Not filtered at all.

Q9 Least Permeability of size & charge of

7nm^- \Rightarrow size of Albumin

7nm^+

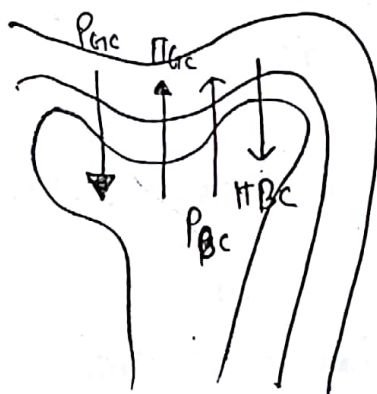
4nm^-

4nm^+ ve

\Downarrow
1st protein to appear in
Urine when basement
Memb. loses its \ominus ve charge.

HCO_3^- free filtered b/c of its small size

* Pressure Responsible for FILTRATION \Rightarrow



Net filtration pressure \Rightarrow

$$\Rightarrow P_{GC} - \pi_{GC} - P_{BC} + \pi_{BC}$$

$$= 45 - 20 - 10 + 0$$

$$= 15\text{mmHg} (\equiv)$$

$$(10\text{mmHg}) (=)$$

* GFR \propto Net filtration pressure

$$\propto (P_{GC} - \pi_{GC} - P_{BC} + \pi_{BC})$$

$$= K_b (\overset{\textcircled{3}}{P_{GC}} - \overset{\textcircled{4}}{\pi_{GC}} - \overset{\textcircled{5}}{P_{BC}} + \overset{\textcircled{6}}{\pi_{BC}})$$

$$\left\{ K_b = \underbrace{\text{Permeability}}_{\textcircled{1}} \times \underbrace{\text{Surface Area}}_{\textcircled{2}} \right.$$

all six parameter affects GFR

* ↑ Sympathetic stimulation



i) Afferent arteriole constriction

ii) Mesangial cell contraction

↳ "KINKING" of Glomerular capillary

↓ S-A
↓ GFR



↓ Surface area

iii) Renin

* In Afferent Arteriole Dilatation



↑ P_{GC}



↑ GFR

* In Ureteric Stone OR Benign Hyperplasia of Prostate



↑ P_{BC}



↓ GFR

Q.Q. Blood Flows from afferent to efferent arteriole,
Which test \Rightarrow

i) P_{GIC}

~~ii) π_{GIC}~~

iii) P_{BC} (Remain Unchanged)

iv) Net filtration pressure

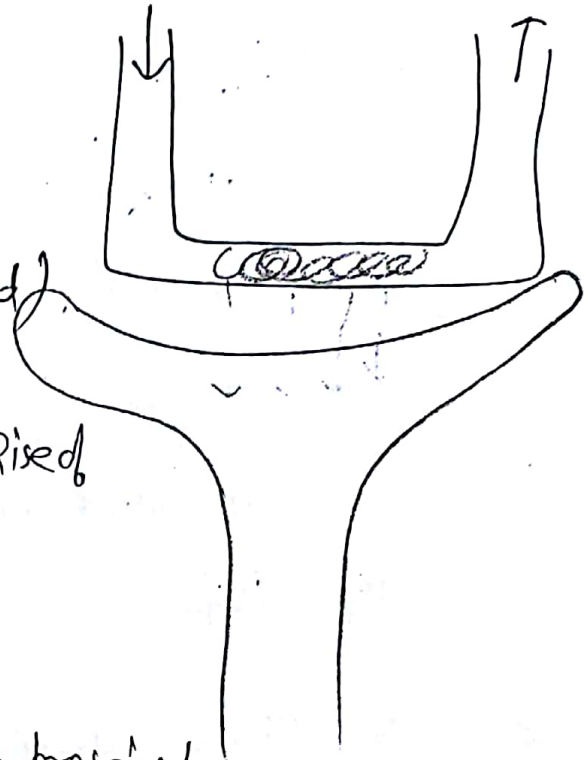
\hookrightarrow does blood rise of

Glomerular filtrate

π_{GIC}

\hookrightarrow Ultrafiltrate of plasma

\hookrightarrow (Plasma - Plasma proteins)



* Sometimes filtration @ the efferent arteriole = 0 (3rd)

\Rightarrow Renal blood flow \Rightarrow 1100 - 1200 mL/min (22-23% of cardiac output)

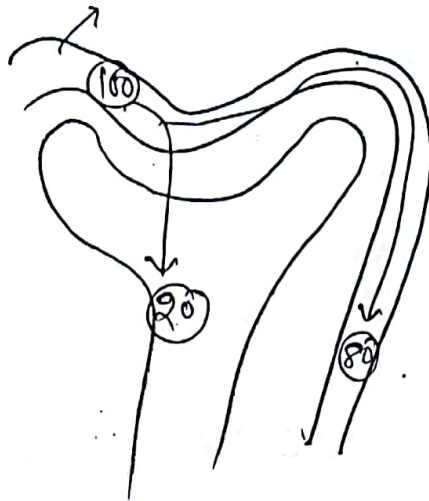
Renal plasma flow \Rightarrow 625 - 650 mL/min

GFR \Rightarrow 125 mL/min

Glomerular filtrate \Rightarrow Ultrafiltrate of plasma

Filtration fraction \Rightarrow $\frac{GFR}{RPF} = \frac{125 \text{ mL/min}}{625 \text{ mL/min}} = 0.16 - 0.20$
 $= 16 - 20 \%$

freely filtered \Rightarrow It doesn't mean 100% filtered



\downarrow
Maximum 20% filtered in
single circulation.

⑧ \uparrow GFR

~~a) Afferent Arteriole dilatation~~

~~b) Efferent Arteriole constriction~~

\downarrow
dual effect on GFR

Mild to
Moderate Efferent
arteriole constriction \Rightarrow

$\uparrow P_{GIC}$
 \uparrow GFR

also \uparrow Filtration
fraction

$\uparrow P_{GIC}$ (also)

At one point $\uparrow P_{GIC}$ More than $\left(\begin{array}{l} \text{In severe efferent} \\ \text{arteriole constriction} \end{array} \right)$
 $P_{GIC} (\uparrow)$; so GFR \downarrow

\downarrow
efferent arteriole diameter is $1/2 - 1/3$
of afferent arteriole diameter
(\downarrow GFR)

⑨

\uparrow Filtration fraction

a) afferent arteriole dilatation

~~b) Efferent arteriole constriction~~

$$FF = \frac{GFR \uparrow}{RPF \uparrow} = \text{Same}$$

$$FF = \frac{GFR \uparrow}{RPF \downarrow}$$

Q0 Effect of ~~Excess~~ arterial constriction on GFR \rightarrow

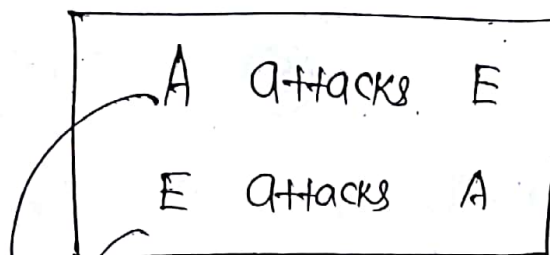
a) ~~Initially~~ \uparrow es then \downarrow es;

b) \uparrow es;

c) \downarrow es;

d) No change.

EFFECT OF ANGIOTENSIN & SYMPATHETIC ON GFR



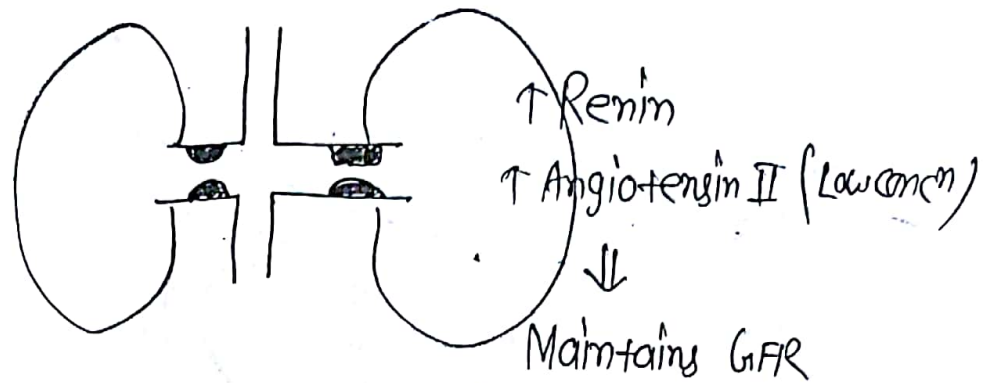
Angiotensin - II \Rightarrow Efferent Arteriole Constriction
Sympathetic (epinephrine) \Rightarrow Afferent Arteriole Constriction (\downarrow GFR)

**

Angio II \rightarrow Low concⁿ \Rightarrow Efferent Arteriole Constriction (\uparrow GFR)
(Physiological condⁿ & Renal A. Stenosis)
 \rightarrow High concⁿ \Rightarrow Both afferent & efferent arteriole constriction (\downarrow GFR)
(Hypovolemia Hemorrhage)

B/L Renal A Stenosis \Rightarrow

80



Pt. comes \bar{c} Hypertension

\hookrightarrow if we give ACE Inhibitor

\Downarrow
It causes to block in Angiotensin II

\Downarrow
Result in "Renal Shutdown"

\rightarrow So; in this patient ACE Inhibitor
all contraindicated.

Renal Handling of different Substances

- Not ^{Filtered} ~~Reabsorbed~~ = Proteins (Albumin)
@ all

- Freely filtered; Not Reabsorb;
Not secreted \Rightarrow

Inulin

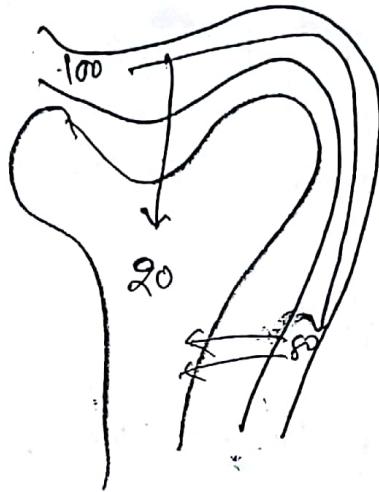
$$Cl_{in} = GFR$$

iii) Freely filtered; Completely Reabsorb \Rightarrow

Glucose

Amino acid

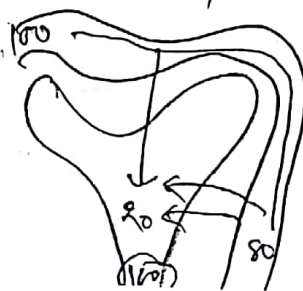
HCO_3^- (if $\text{HCO}_3^- < 24 \text{ meq/Litre}$)



iv) Freely Filtered ; Partly Reabsorb \Rightarrow

$\text{H}_2\text{O} \Rightarrow \text{GFR} \Rightarrow 180 \text{ Litres/day}$
 $\text{Urine} \Rightarrow 1 - 1.5 \text{ Litre/day}$
 Electrolytes
 Urea (52%)

v) Freely filtered; completely secreted \Rightarrow



Para amino hippuric acid

\Downarrow
Renal plasma flow

PAH (low concn)

vi) Freely filtered; Partially secreted \Rightarrow

(81)

PAH (High concn)

creatinine

* How to calculate the filtration Rate & Excretion Rate:

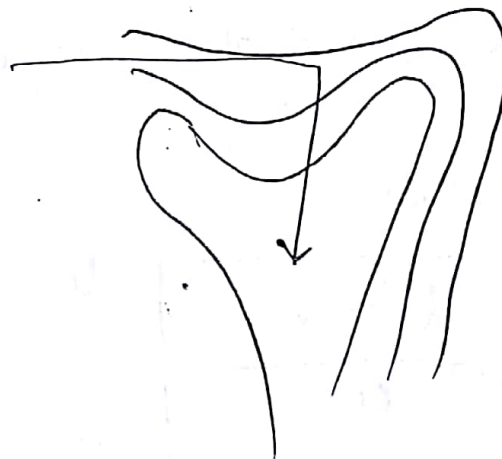
Filtration Rate



GFR \times P_{Xx}

$\frac{ml}{min} \times \frac{mg}{ml}$

$= \frac{mg}{min}$



Excretion Rate



$U_x \times V$ Rate of
 \Downarrow Urine concn of "X" urine flow

$= \frac{mg}{ml} \times \frac{ml}{min}$

$= \frac{mg}{min}$

QA - Blood glucose = 100 mg/dl = 1 mg/mL

GFR = 100 mL/min

1 mg/min

10 mg/min

~~100 mg/min~~

100,00 mg/min

Q9

$$Na^+ = 140 \text{ mg/L}$$

$$GFR = 180 \text{ L/day}$$

filtration Rate / day

$$= 180 \times 140 = 25,200 \text{ mg/day}$$

CLEARANCE **

- Volume of plasma cleared of that substance / free of that substance in unit time \rightarrow clearance of substance

- Unit \Rightarrow mL/min.

$$Cl_x = \frac{U_x \times V}{P_x}$$

U_x = Urinary concⁿ of substance "x" (mg/mL)

V = Rate of urine flow (mL/min)

P_x = Plasma concⁿ of "x" (mg/mL)

**

$$[Cl_x] = \frac{\frac{\text{mg}}{\text{mL}} \times \frac{\text{mL}}{\text{min}}}{\frac{\text{mg}}{\text{mL}}} = \frac{\text{mL}}{\text{min}}$$

$$Cl_{\text{Inulin}} = \text{GFR}$$

82

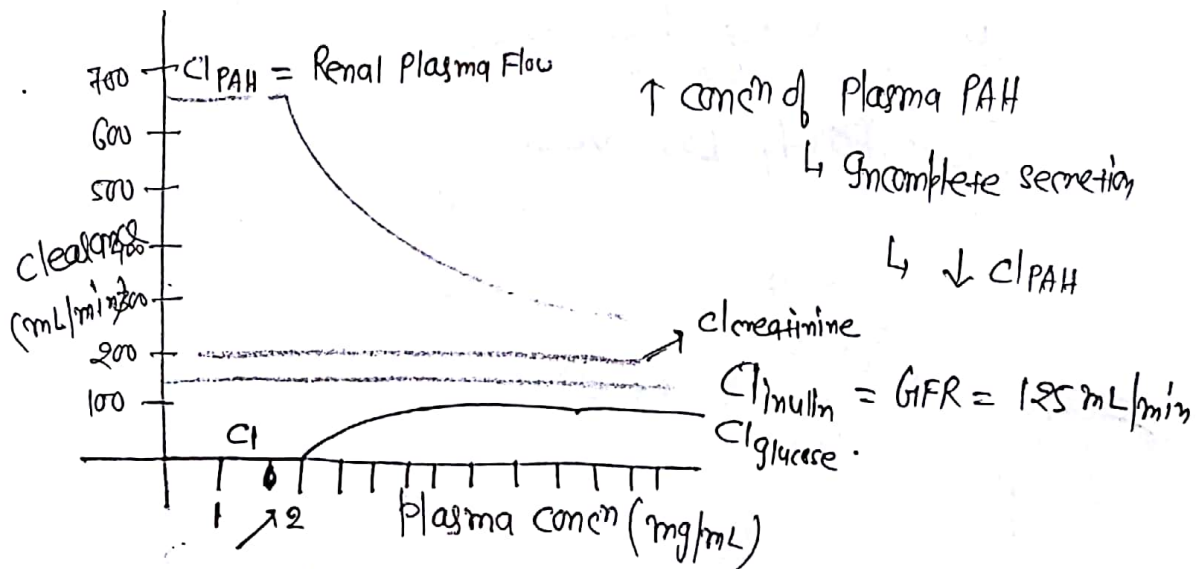
$$Cl_{\text{PAH}} (\text{in Low concn}) = \text{Renal Plasma flow}$$

For Inulin \Rightarrow Filtration Rate = Excretion Rate

$$\Rightarrow \text{GFR} \times P_{\text{in}} = U_{\text{in}} \times V$$

$$\Rightarrow \text{GFR} = \frac{U_{\text{in}} \times V}{P_{\text{in}}}$$

$$\Rightarrow \text{GFR} = Cl_{\text{Inulin}}^*$$



Renal threshold
(180-200 mg/dl)
OR

2 mg/mL

below 2 mg/mL $Cl_{\text{glucose}} = 0$; b/c urinary concn of glucose is zero below 2 mg/mL.

Q. Q. Which of the following has highest clearance?

a) Inulin;

b) Glucose;

c) Urea;

d) Creatinine

Q. Q. Cl_{PAH} is used for Measurement of Renal Plasma flow. Technician by Mistake; gives 3 times Recommended dose of PAH

(a) N value

(b) Falsely high value

(c) Falsely Low value

FREE H₂O CLEARANCE

$$Cl_{H_2O} = \frac{\text{Rate of clearance of osmoles}}{\text{Urine flow } (\dot{V})}$$

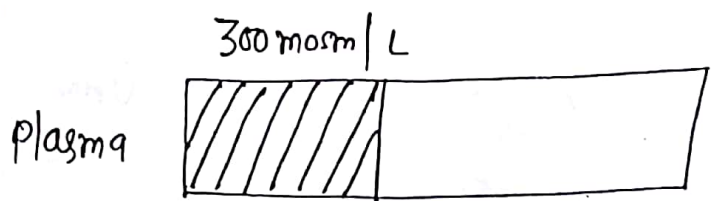
$$Cl_{H_2O} = \dot{V} - \left[\frac{U_{osm} \times \dot{V}}{P_{osm}} \right]$$

* if Urine is isotonic w.r.t. plasma \Rightarrow

$$Cl_{H_2O} = \dot{V} - \left[\frac{U_{osm} \times \dot{V}}{P_{osm}} \right]$$

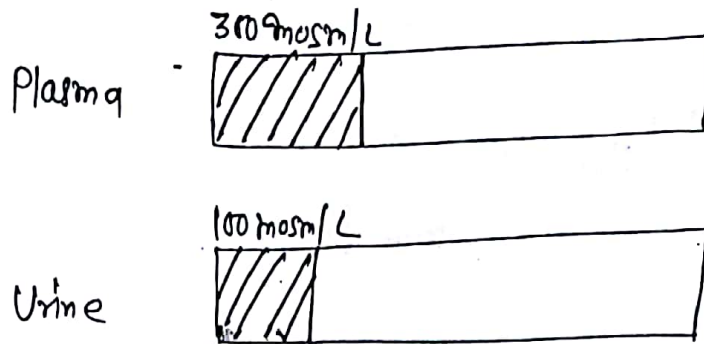
$$= \dot{V} - \dot{V}$$

$$= \text{Zero}$$



$$C_{H_2O} = \text{Zero}$$

* if Urine is Hypotonic \Rightarrow



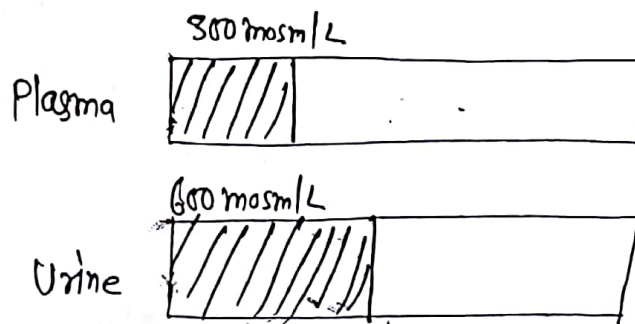
$$C_{H_2O} = \dot{V} - \frac{100 \times \dot{V}}{300}$$

$$C_{H_2O} = \oplus ve$$

$$= \dot{V} - \frac{1}{3} \dot{V}$$

$$= \frac{2}{3} \dot{V}$$

* if Urine is hypertonic / concentrated \Rightarrow



$$C_{H_2O} =$$

$$\dot{V} - \left(\frac{600 \times \dot{V}}{300} \right)$$

$$= \dot{V} - 2\dot{V} = -\dot{V}$$

$$C_{H_2O} = \ominus ve$$

Q.

$$C_{H_2O} = -1.2 \text{ ml/min}$$

Urine is

- ↳ (a) Isotonic
- (b) Hypotonic
- ~~(c) Hypertonic~~

Q.

In Diabetes Insipidus, $C_{H_2O} = 11$

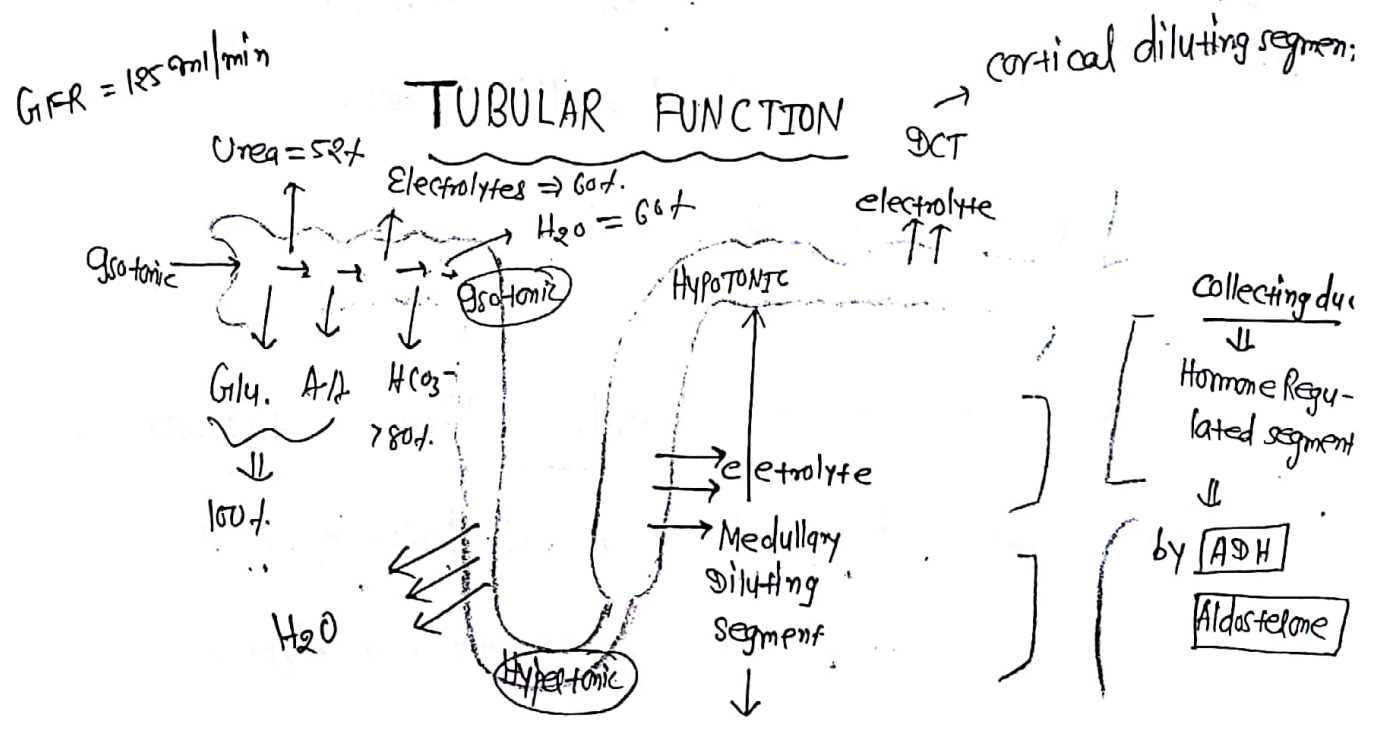
⊕ve; ↑es

Q.

Marathon Runner ; Sweating ⊕⊕

Max^m Antidiuresis ; $C_{H_2O} = 11$

- (a) ⊕ve; (b) ~~⊖ve~~



PCT \Rightarrow Angiotensin II \Rightarrow \uparrow Na^+ Reabsorption

PTH \rightarrow \downarrow Phosphorus Reabsorption

(Phosphaturic Action of PTH)

TAL $\xrightarrow{\text{Thick ascending Limb}}$

\Rightarrow Angiotensin II \rightarrow \uparrow Na^+ Reabsorption

DCT \Rightarrow PTH \Rightarrow \uparrow Ca^{2+} Reabsorption

CD \Rightarrow ADH \Rightarrow \uparrow H_2O Reabsorption

Aldosterone \Rightarrow \uparrow Na^+ Reabsorption

\uparrow K^+ Secretion

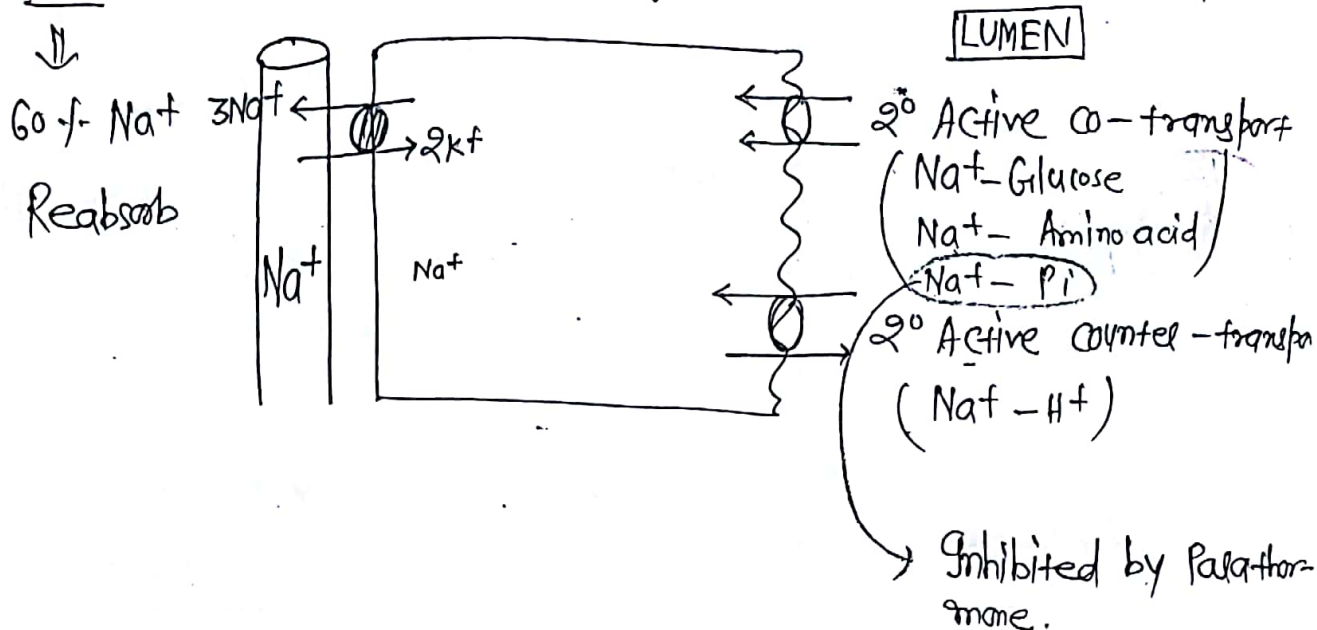
\uparrow H^+ Secretion

ANP \Rightarrow \downarrow Na^+ Reabsorption

* How does kidney handle different substances \Rightarrow

SODIUM \Rightarrow Reabsorbed in all parts of Nephron
except \Rightarrow Descending thin segment

PCT \Rightarrow Basolateral side of PCT has $\text{Na}^+ - \text{K}^+$ Pump.



In PCT,

$\text{Na}^+ - \text{P}_i$ IIa protein

$\text{Na}^+ - \text{P}_i$ IIc protein

\rightarrow This protein is inhibited by PTH



\uparrow Urinary loss of inorganic phosphorus

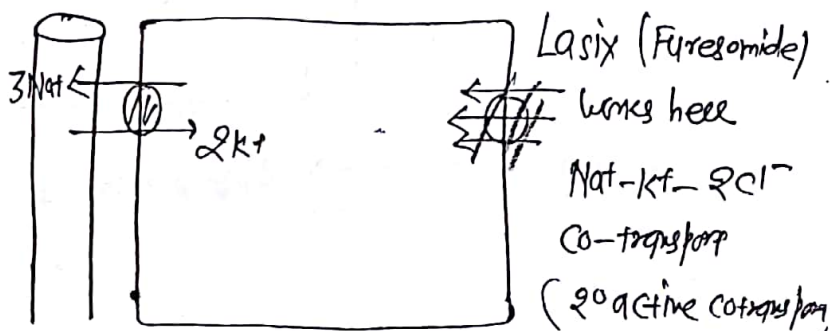
(Phosphaturic action of PTH)

Descending thin segment \Rightarrow No Reabsorption of Na^+

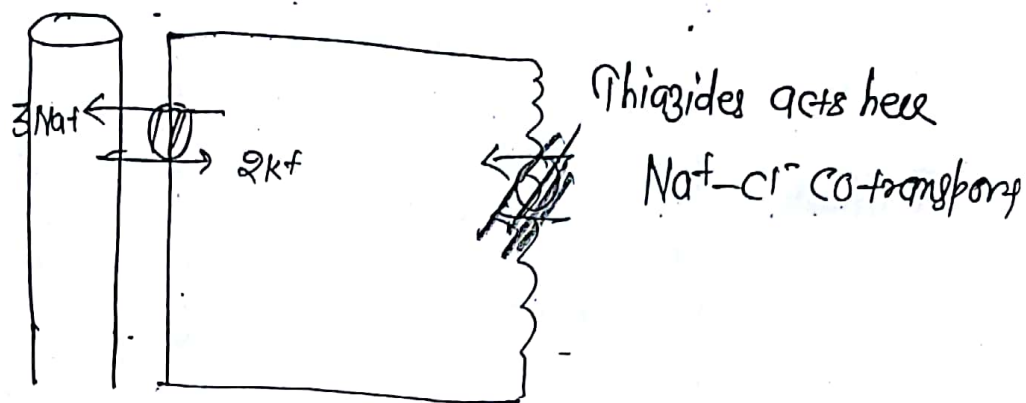
Thick Ascending Limb \Rightarrow

\Downarrow

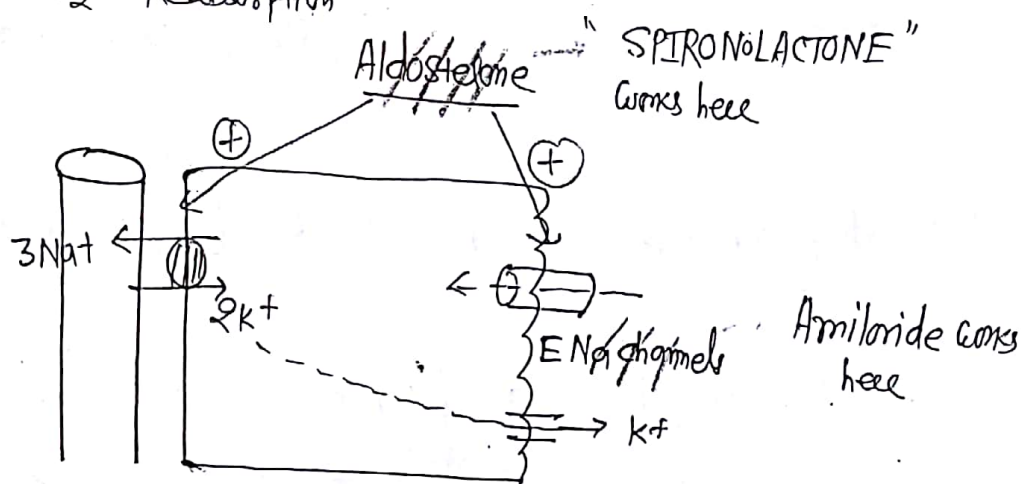
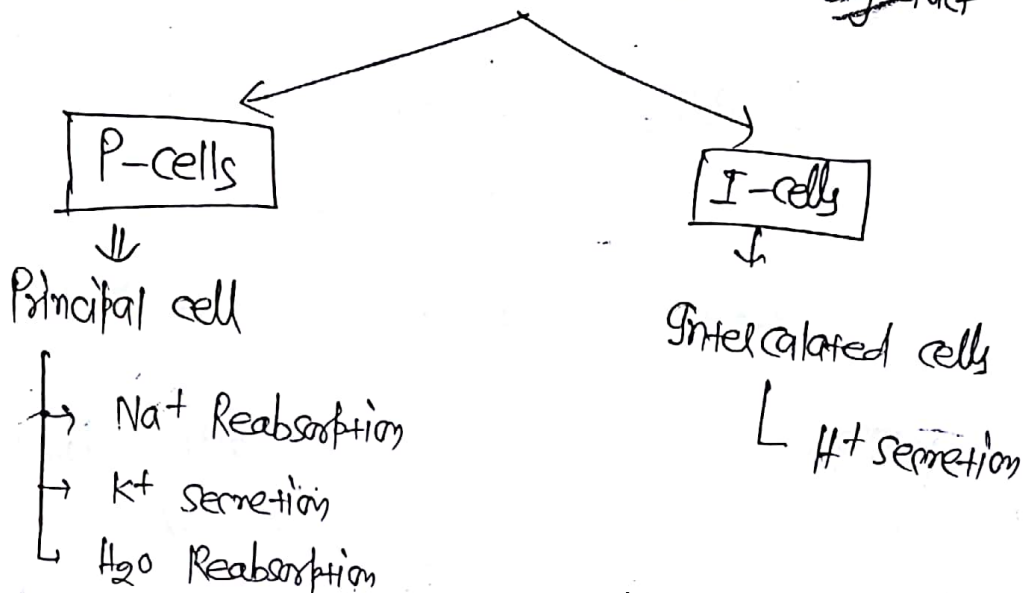
30% Na^+ Reabsorb



DCT \Rightarrow 7% Na^+ Reabsorbed



\rightarrow Secreted by Zona glomerulosa of Adrenal cortex.
 Aldosterone acts on Late DCT & collecting duct



RAAS \Rightarrow Aldosterone \Rightarrow \uparrow Na^+ Reabsorption
 \uparrow K^+ secretion
 \uparrow H^+ secretion (by "I-cells")

Q which gives directly stimulation to Aldosterone??

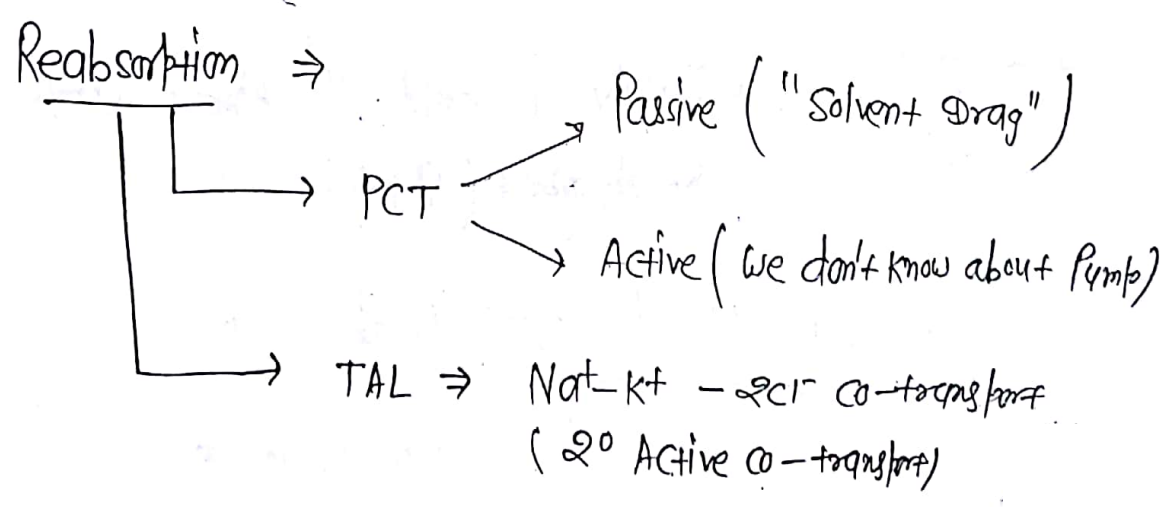
- (a) $\uparrow Na^+$:-
- (b) $\downarrow Na^+$; (it works via RAAS)
- ~~(c) $\uparrow K^+$;~~
- (d) $\downarrow K^+$

Q Hyperaldosteronism can never cause??

Likely to cause

- ~~a) Acidosis;~~
- b) Alkalosis;
+
Hypokalemia

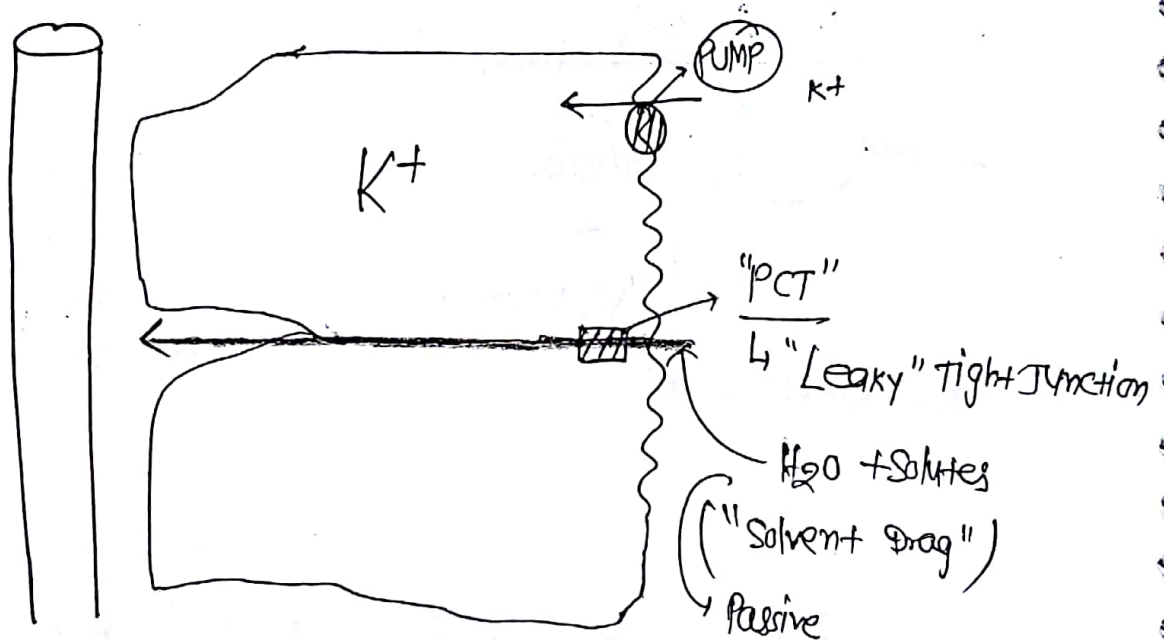
POTASSIUM \Rightarrow It is both Reabsorbed & Secreted. (Q)



Secretion

↳ Collecting duct & Late DCT
(by Aldosterone)

SOLVENT DRAG ⇒



CALCIUM ⇒ Freely filtered & Almost completely Reabsorbed (99+)

— Mechⁿ of Ca^{+2} Reabsorption

↳ Similar to Na^+

— Max^m Ca^{+2} Reabsorption ⇒ PCT

* PTH \uparrow Ca^{2+} Reabsorption in "DCT"

(87)

MAGNESIUM \Rightarrow Max^m Mg^{2+} Reabsorption in "Thick Ascending Limb"

- Lasix \rightarrow \uparrow Urine loss of - Na⁺

Cl^-

K^+

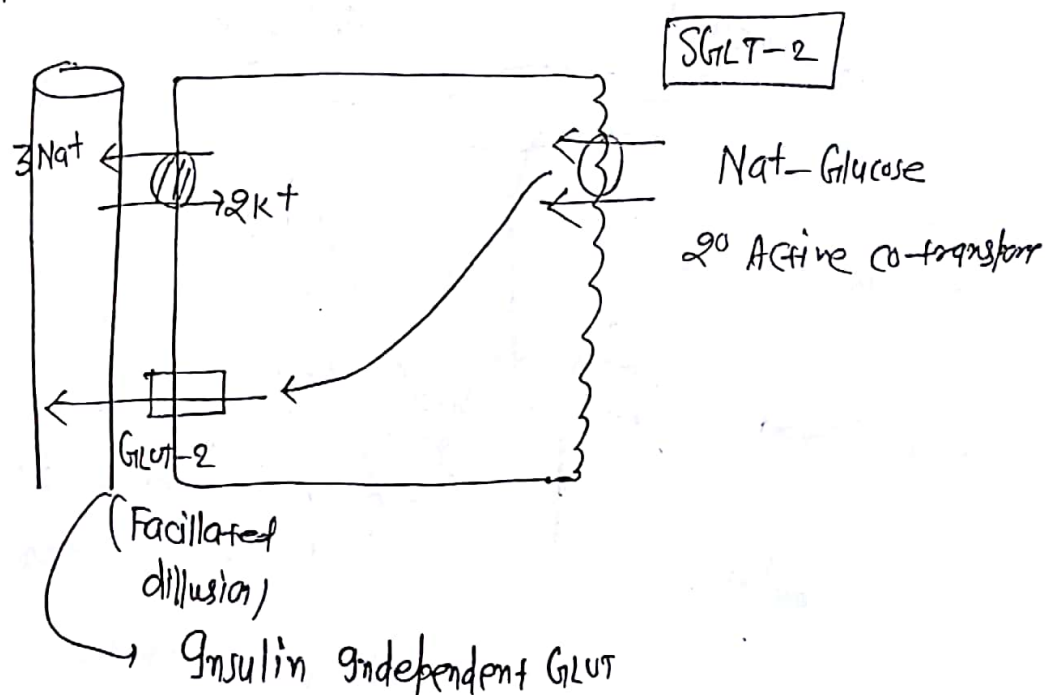
Ca^{2+}

Mg^{2+}

GLUCOSE

Site = PCT ; 100% Reabsorption

Mechanism \rightarrow



RENAL THRESHOLD

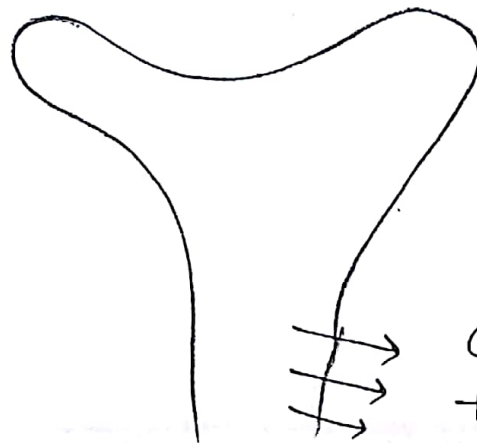
⇒ Plasma concⁿ beyond which
Glucose appears in urine



180-200 mg/dl

OR

2 mg/mL



Carrier Mediated
transport

Gl's Rate^{*}



T_{mG}



Transport Maxima
of Glucose

♂ = 375 mg/min

♀ = 300 mg/min

*

Renal threshold



2 mg/mL

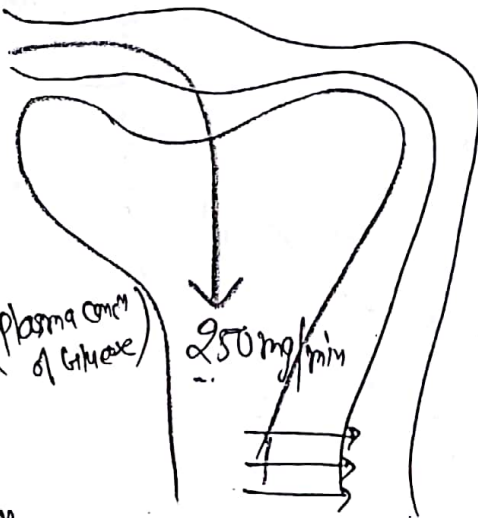
Filtration Rate



GFR × P_{Glucose} (Plasma concⁿ
of Glucose)

= 125 × 2

= 250 mg/min



$T_{mG} = 375 \text{ mg/min (♂)}$
 $= 300 \text{ mg/min (♀)}$

Ideally @ this condⁿ total glucose Reabsorbed & (88)
 Not appear in urine; but b/c of

"NEPHRON HETEROGENEITY"

All Nephron's Not
 work simultaneously and
 Not e same capacity;

↳ At Plasma glucose of 2mg/mL
 - ↳ Filtration Rate of
 Glucose is 250 mg/min; which is
 less than T_{Mg} ; but at P_{Glu} of
 2mg/mL → Glucose begins to appear
 in urine

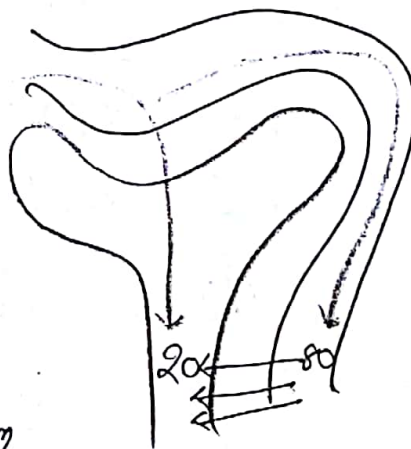
PAH

- Freely filtered & completely secreted (In Low concⁿ)

PAH (Low concⁿ)
 $< 20 \text{ mg/dl}$ ⇒

if ↑ Plasma concⁿ of
 PAH
 ↓
 Incomplete secretion

↳ clearance PAH ↓



Secretion of PAH

↳ PCT
 ↳ carrier mediated
 secretion
 ↳ $T_{m} \oplus$

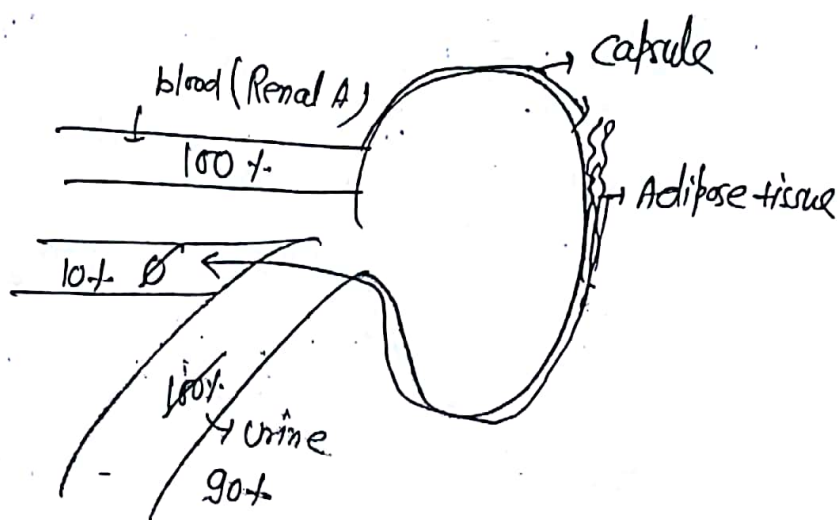
$(T_m)_{PAH} = 80 \text{ mg/min}$

Q Q

PAH (Low concⁿ)



So, PAH has an
Extraction Ratio



$$\text{Extraction Ratio} = \frac{\text{Arterial conc}^n - \text{Venous conc}^n}{\text{Arterial conc}^n}$$

$$= \frac{100 - 10}{100} = \frac{90}{100} = 0.9 \text{ OR } 90\%$$

Why there is an Extraction Ratio of PAH??

b/c complete Renal Artery blood doesn't participate in filtration (Small amount goes into Renal capsule & Adipose tissue & directly goes into Renal vein, Not participate in filtration).

Q Q

Cl_{PAH} (Low concⁿ) (A) Actual Renal blood flow

(B) Effective Renal blood flow

(C) Actual Renal Plasma flow (ARPF)

~~(D) Effective Renal Plasma flow (ERPF)~~

$$\boxed{\text{ARPF} = \frac{\text{ERPF}}{0.9}}$$

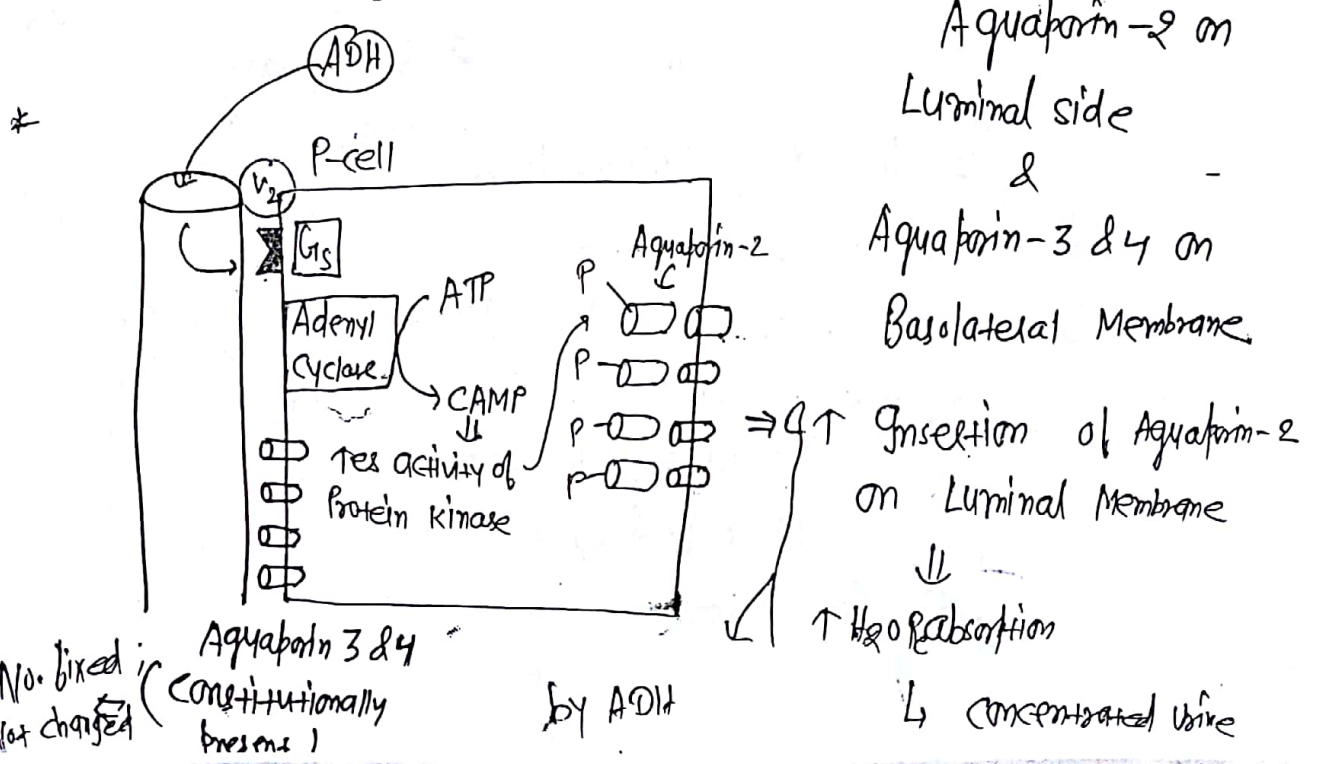
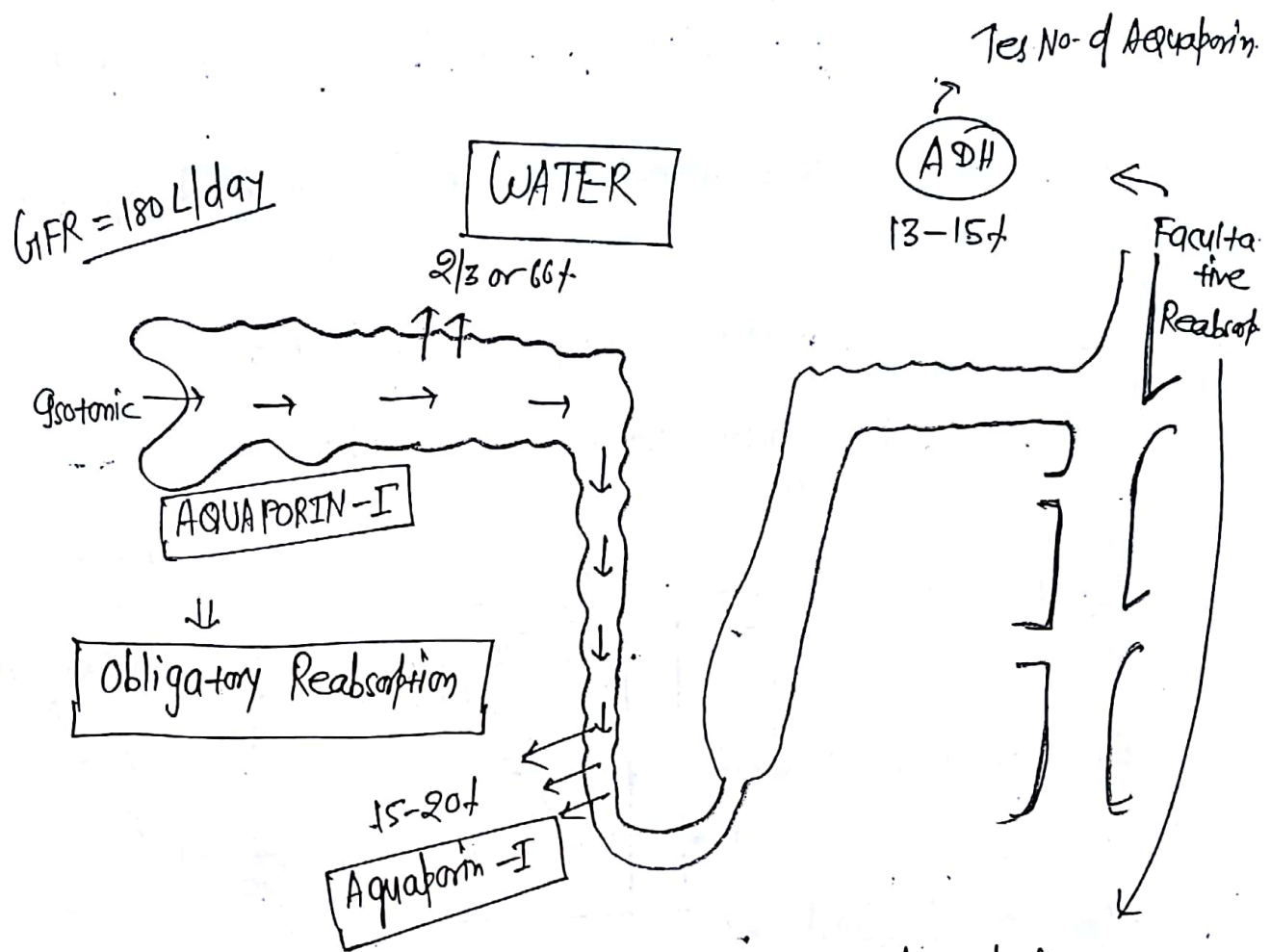
Q Q ERPF = 63 ml/min

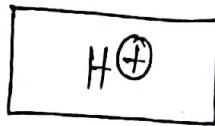
ARPF = 91

ARPF = 700 ml/min

**

$$\text{Renal blood flow} = \frac{100}{100 - \text{Hematocrit}} \times \text{Renal Plasma Flow}$$





Filtration \longrightarrow Not possible
 b/c No free form H^+ .

\hookrightarrow but urine is acidic ; b/c of secretion of H^+

Q. Maxm H^+ is secreted by -

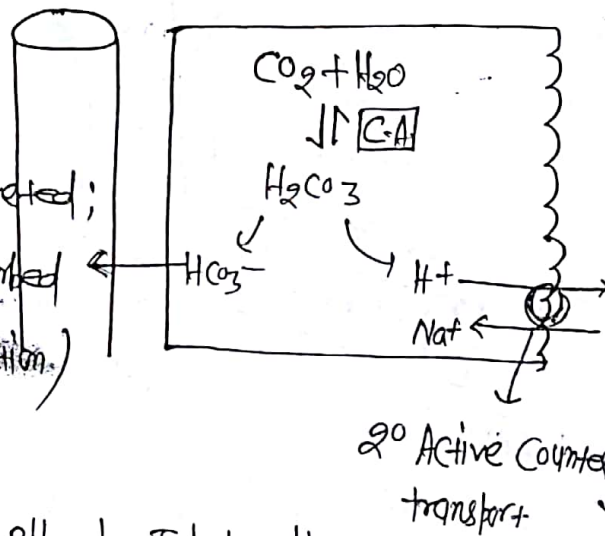
- ~~(a) PCT (4200 mmol/day)~~
- (b) CD (<80 mmol/day)

Q. Urinary Acidification occurs by -

- (a) PCT
- ~~(b) CD~~

In PCT \hookrightarrow

For every H^+ secreted;
 $\uparrow HCO_3^-$ is Reabsorbed
 (Indirect Reabsorption)



Lumen
 Cells Rich in
 Carbonic Anhydrase
 \downarrow
 PCT
 RBCs
 Parietal cell of
 Stomach

Q. What is the pH of Tubular fluid

(a) the end of PCT;

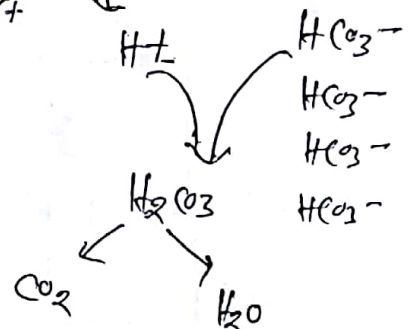
- ~~(a) 7.3 (No change in pH)~~

(b) 6.3

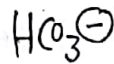
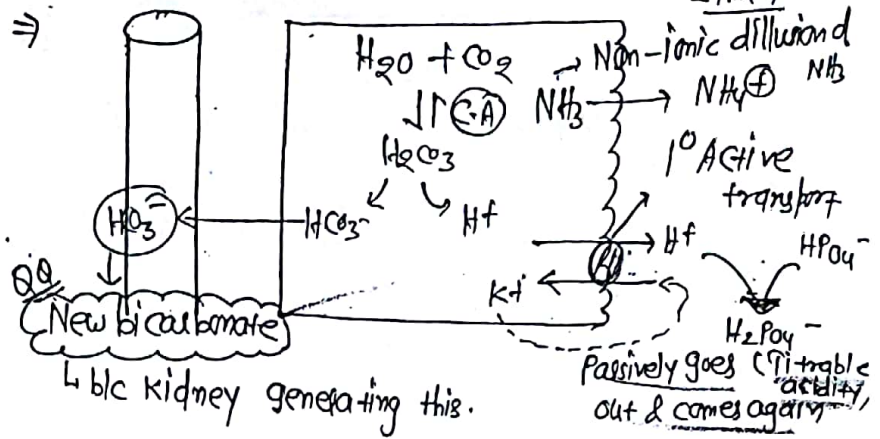
(c) 5.3

(d) 4.3

\downarrow
 b/c whatever H^+ secreted
 is buffered by HCO_3^-



In collecting duct \Rightarrow
(I-cells)



80% Reabsorb in PCT
TAL DCT] 20% Reabsorb

Mech^m \Rightarrow Same as in PCT

So; as we enter collecti. duct; No HCO_3^- is there
So; Now H^+ buffered by HPO_4^-

Urinary buffers \Rightarrow

- ① HCO_3^- (bicarbonate)
- ② HPO_4^{2-} (phosphate)
- ③ NH_3 (Inducible urinary ⁹⁰buffer)

b/c in Acidosis \Rightarrow \uparrow NH_3 production.

Limiting pH of Urine \Rightarrow pH = 4.5

Factors which affect H^+ secretion \Rightarrow

- ① Pco_2
- ② Aldosterone \rightarrow \uparrow H^+ secretion in collecting duct
- ③ Carbonic Anhydrase Inhibitor
 \rightarrow \downarrow H^+ secretion
 \rightarrow \uparrow Urinary loss of

Causes Acidosis
 \downarrow
eg: Acetazolamide

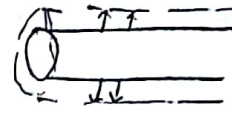
\downarrow Na^+
 \downarrow HCO_3^-
 \downarrow H_2O (so causes diuresis)

REGULATION OF SODIUM EXCRETION & GFR

① Myogenic Mechⁿ of Autoregulation of GFR →

B/w MAP of 90 & 200 mm Hg ⇒ GFR is constant.

* ↑ Renal blood flow



↑ Stretch

opening of Mechano-Sensitive Ca²⁺ channel

Ca²⁺ Influx

Vascular Smooth Muscle contraction

So, GFR constant

So, GFR constant

eg of Negative Feedback

② Tubuloglomerular feedback (TGF) ⇒

↑ GFR

↑ Na⁺, Cl⁻ Load in tubular fluid

act as sensor

Macula densa

Macula Densa

↑ Na⁺, Cl⁻ Reabsorption by Macula densa cells

Increase Na⁺, Cl⁻ reabsorption by Macula densa cells

↑ Activity of Na⁺ K⁺ ATPase Pump

Increase activity of Na⁺ K⁺ ATPase pump

Vasoconstriction of Afferent Arteriole

site of action

pt. in vascular Smooth Muscle

Receptor

↑ Adenosine

Increase adenosine

↑ ATP Hydrolysis

Juxta Glomerular Apparatus \Rightarrow

① JG cells JG Cells

- Renin secreting cells
- In tunica media of afferent arteriole \gg efferent arteriole

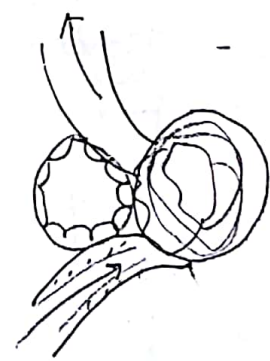
Macula densa cell

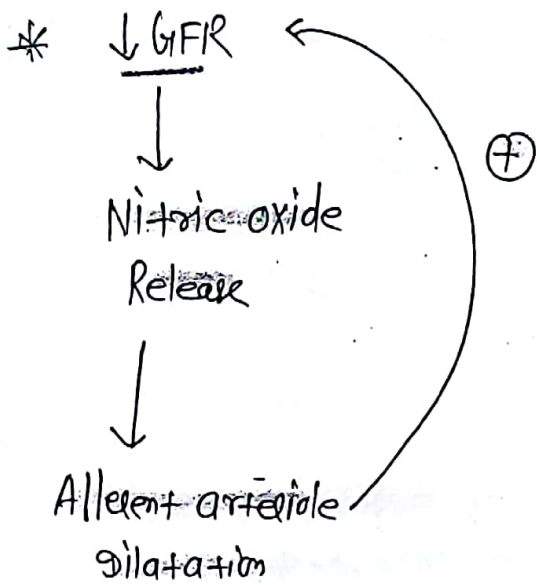
② Macula densa cells \Rightarrow pr. @ beginning of DCT

- Modified Tubular epithelial cells pr. @ the end of Loop of Henle = the end of loop of Henle
- It is " SENSOR "
- Detect Nat & cr Load in Tubular fluid

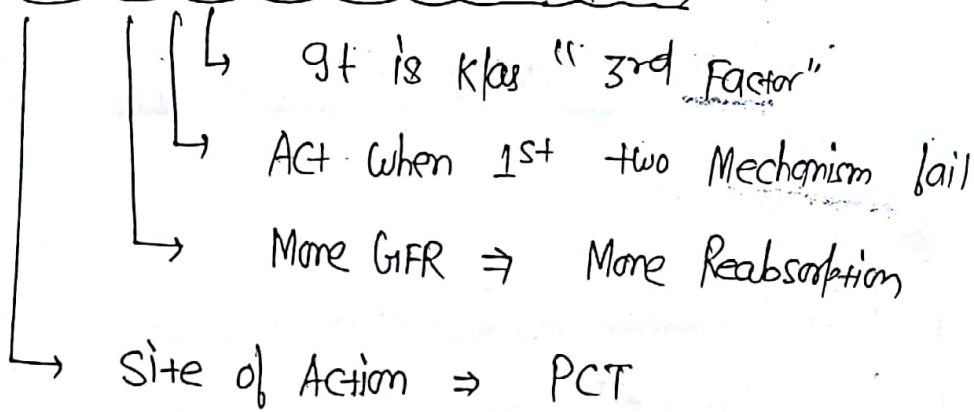
③ Laci's cells Laci's cells

- extraglomerular Mesangial cells ectraglomerular mesangial cells
- We don't know about exact Role
- It take up immune complexes in certain type of Glomerular Nephritis

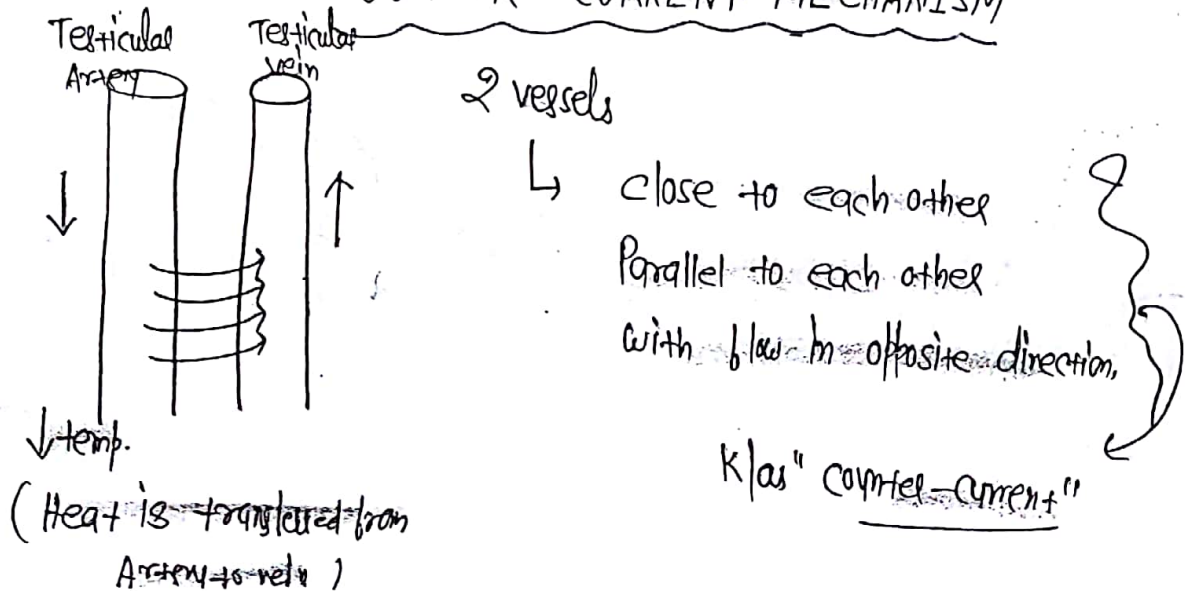




③ Glomerulo-tubular Balance (GTB)



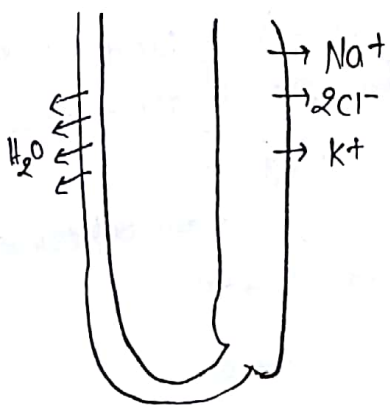
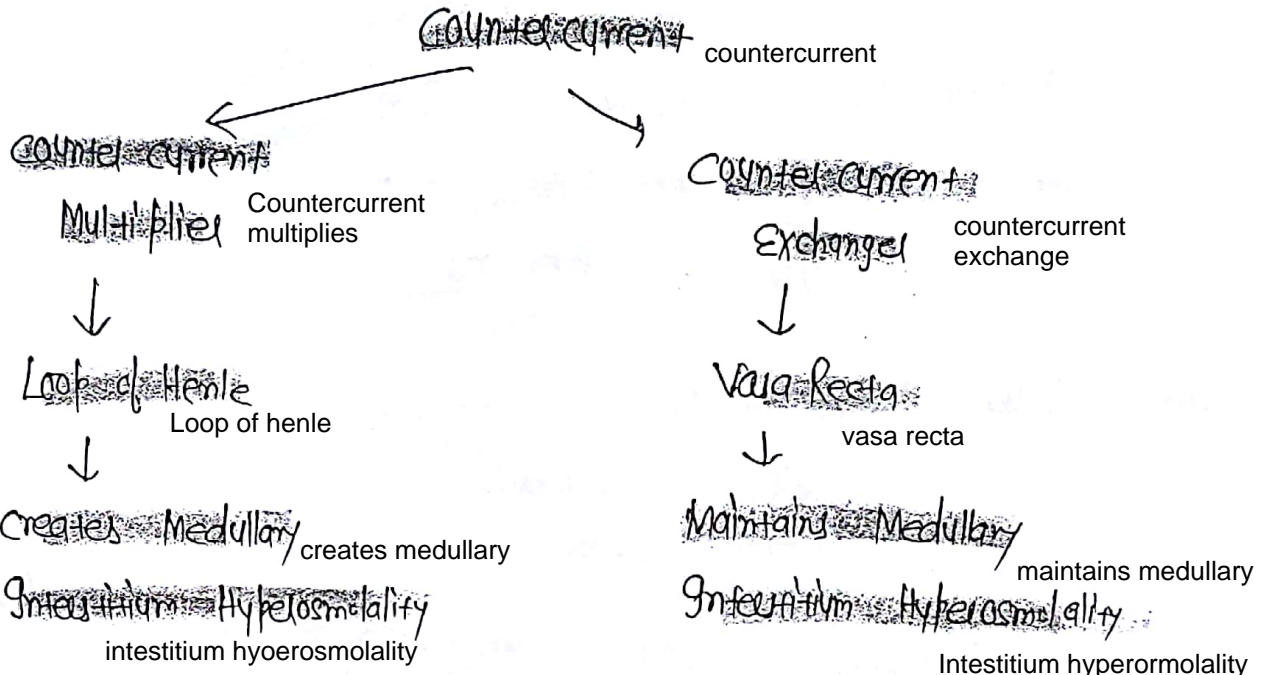
COUNTER-CURRENT MECHANISM



prt. in

- ~~Kidney~~ Kidney
- ~~Testicular vessels~~ Testicular vessels
- ~~Intestinal villi~~ Intestinal villi
- ~~Venae comitantes~~ Venae comitantes

~~Pair of veins a/q certain arteries~~
Pair of veins a/q certain arteries
~~help to conserve heat~~
Help to conserve heat



~~2 Limbs of Loop of Henle~~

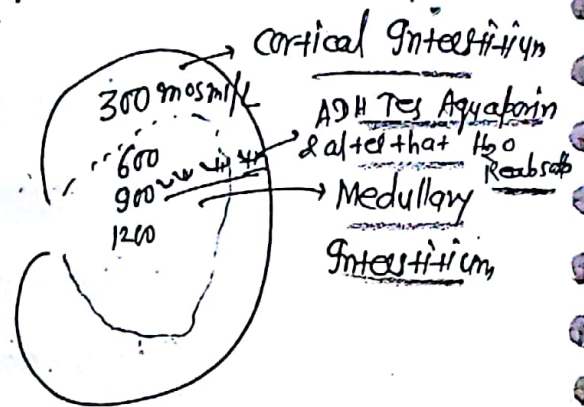
↳ ~~differential~~

~~Permeability~~ Differential permeability

to produce a concⁿ Urine; we Need



- ① ADH
- ② Medullary Interstitial hyperosmolality



both are Must for concⁿ Urine;
if Any one absent; No concⁿ Urine formed

Qa Max^m Urine Osmolality \Rightarrow 1200 mOsm/L

Qa Possible Range of Urinary Osmolality \Rightarrow

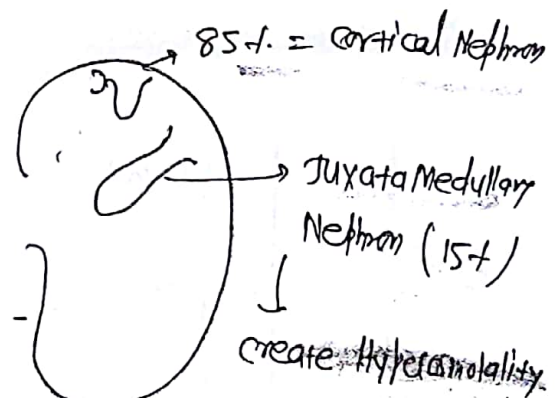
~~50~~ — ~~1200~~ mOsm/L
ADH Max^m ADH

Qa Usual Range of Urinary Osmolality \Rightarrow

~~300~~ — ~~1200~~ mOsm/L
Isotonic Hypertonic

* Solutes Responsible for Medullary Interstitium Hyperosmolality \Rightarrow

Major $\leftarrow \left\{ \begin{array}{l} \text{Na}^+ \\ \text{K}^+ \\ \text{Cl}^- \end{array} \right\}$ TALE

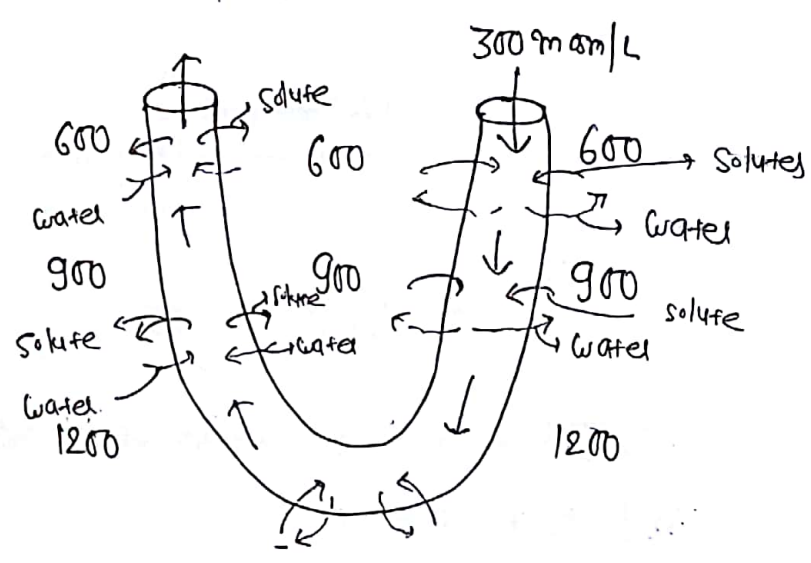
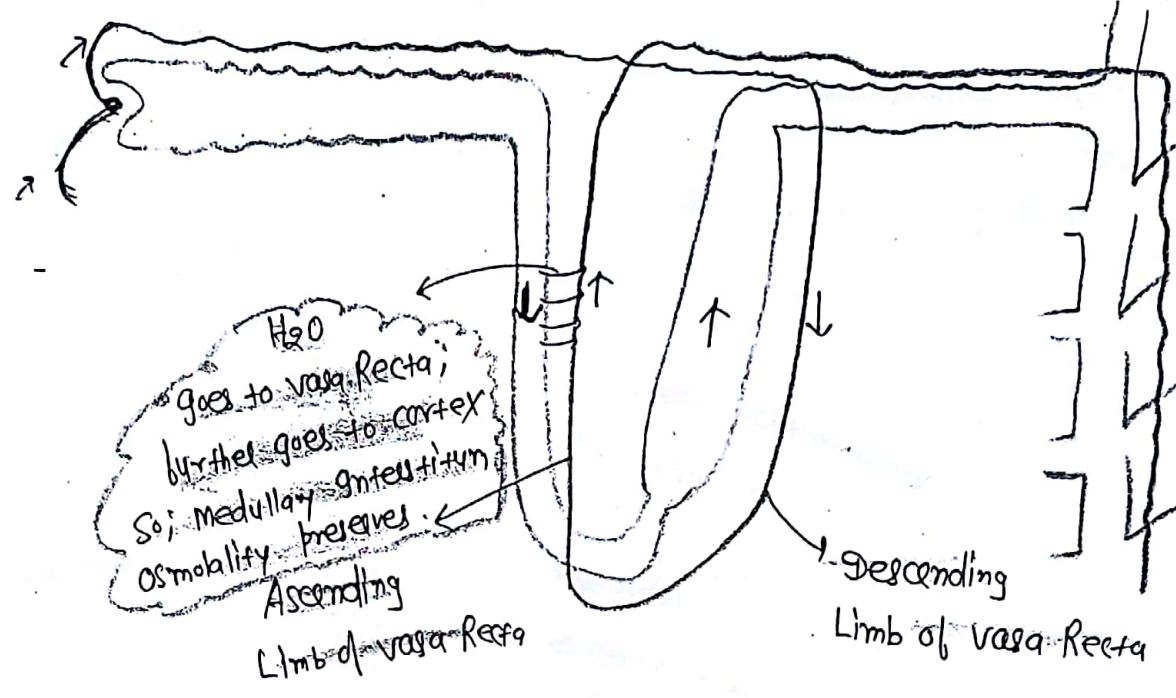


Minor \leftarrow Urea from Medullary collecting duct

* Urea is ~~Reabsorb~~ \Rightarrow PCT but comes to PCT; but comes to

Medullary Interstitium & some time medullary interstitium and sometime contribute 50% of Medullary Interstitium hyperosmolality
contribute 50% of medullary interstitium hyperosmolality

* 1st part of kidney affected by Anoxia \Rightarrow Medulla
 (b/c of preserved Loop of Henle)



RESPIRATORY SYSTEM

(93)

BRONCHODILATION

- * ~~Sympathetic stimulation~~
sympathetic stimulation
- * ~~Adrenergic agents~~
Adrenergic agents
- * Adrenaline
- * VIP (By ~~NANC~~ ^{↳ Nerves})
Non-Adrenergic
Non-Cholinergic
↓
Bronchial Smooth Muscle Relaxant

BRCHOCONSTRICTION

- * ~~Parasympathetic stimulation~~
Parasymp. stimulation
- * ACh
- * Cholinergic Agents
- * Leukotrienes
- * Substance P
- * Adenosine
- * Cool Air

* Total Pulmonary Ventilation $\Rightarrow R.R. \times T.V$ ^{Respiratory Rate} _{Pidal volume}

Alveolar Ventilation $\Rightarrow R.R. \times (T.V - D.S.)$

DEAD SPACE (D.S)

Volume of Air which doesn't participate in Respiratory Exchange

- * In Infants $\Rightarrow 3.3 \text{ ml/kg body weight} = 15-30 \text{ ml}$
- In Adults $\Rightarrow 2 \text{ ml/kg body weight} = 140-150 \text{ ml}$

Physiological OR Total Dead space = Anatomical dead space + Wasted Ventilation

* ~~Wasted~~ Ventilation \Rightarrow

$$\frac{V}{Q} > 1$$

i.e. ventilation is in excess of Perfusion; & this ventilation is going to be wasted.

Overventilated alveoli

Underperfused alveoli

* $V/Q > 1.0$

\downarrow ventilation
wasted ~~perfusion~~

\downarrow
Physiological
Dead space

eg \Rightarrow Thrombus in
vessels

$V/Q < 1.0$

\downarrow
wasted Perfusion

\downarrow
Incomplete oxygenation of
blood

\downarrow
Klas "Shunting of blood"

eg \Rightarrow Foreign body

* In (N) Individual ; wasted ventilation $\Rightarrow 0$

\downarrow
So; in (N) Individual ;

Physiological D.S. = Anatomical D.S.

Measure by "BOHR's Equation" &

\downarrow of CO_2
Partial Pressure in Expired Air (P_{E,CO_2})
 \downarrow of CO_2
Partial Pressure in Arterial blood (P_{a,CO_2})
Tidal volume (V_T)

Measure by FOWLER'S TECHNIQUE

\downarrow
Measured N_2 analysis in expired
Air After single deep breath
of 100% O_2

Bohr's Eqn $\Rightarrow P_{E\text{CO}_2} \times V_T = P_{a\text{CO}_2} \times (V_T - V_D)$ (96)
 \downarrow dead space volume.

Q9 $P_{E\text{CO}_2} = \text{given}$
 $P_{a\text{CO}_2} = \text{given}$

$\frac{V_D}{V_T}$ Ratio

$$P_{E\text{CO}_2} \times V_T = P_{a\text{CO}_2} \times (V_T - V_D)$$

$$\Rightarrow \frac{P_{E\text{CO}_2}}{P_{a\text{CO}_2}} = \frac{V_T - V_D}{V_T}$$

$$= \frac{P_{E\text{CO}_2}}{P_{a\text{CO}_2}} = 1 - \frac{V_D}{V_T}$$

$$\Rightarrow \left\{ \frac{V_D}{V_T} = 1 - \frac{P_{E\text{CO}_2}}{P_{a\text{CO}_2}} \Rightarrow \frac{P_{a\text{CO}_2} - P_{E\text{CO}_2}}{P_{a\text{CO}_2}} \right\}$$

(N) Ratio is upto 0.4

SPIROMETRY

LUNG VOLUMES & CAPACITY

TIDAL VOLUME \Rightarrow Volume of Air Inspired OR Expired during a Normal quiet Respiration.

- Only volume which is same in Male & Female

- 500 mL.

INSPIRATORY RESERVE VOLUME \Rightarrow Volume of Air Inspired forcefully;
over & above a tidal inspiration; with
Max^m effort.

3300 ml = σ

1900 ml = ♀

EXPIRATORY RESERVE VOLUME \Rightarrow Volume of Air expired forcefully;
over & above a tidal expiration; with Max^m
effort.

- 1200 ml = σ

700 ml = ♀

Residual volume \Rightarrow Volume of Air which Remains in Lung
at the end of Max^m expiration

- 1200 ml = σ

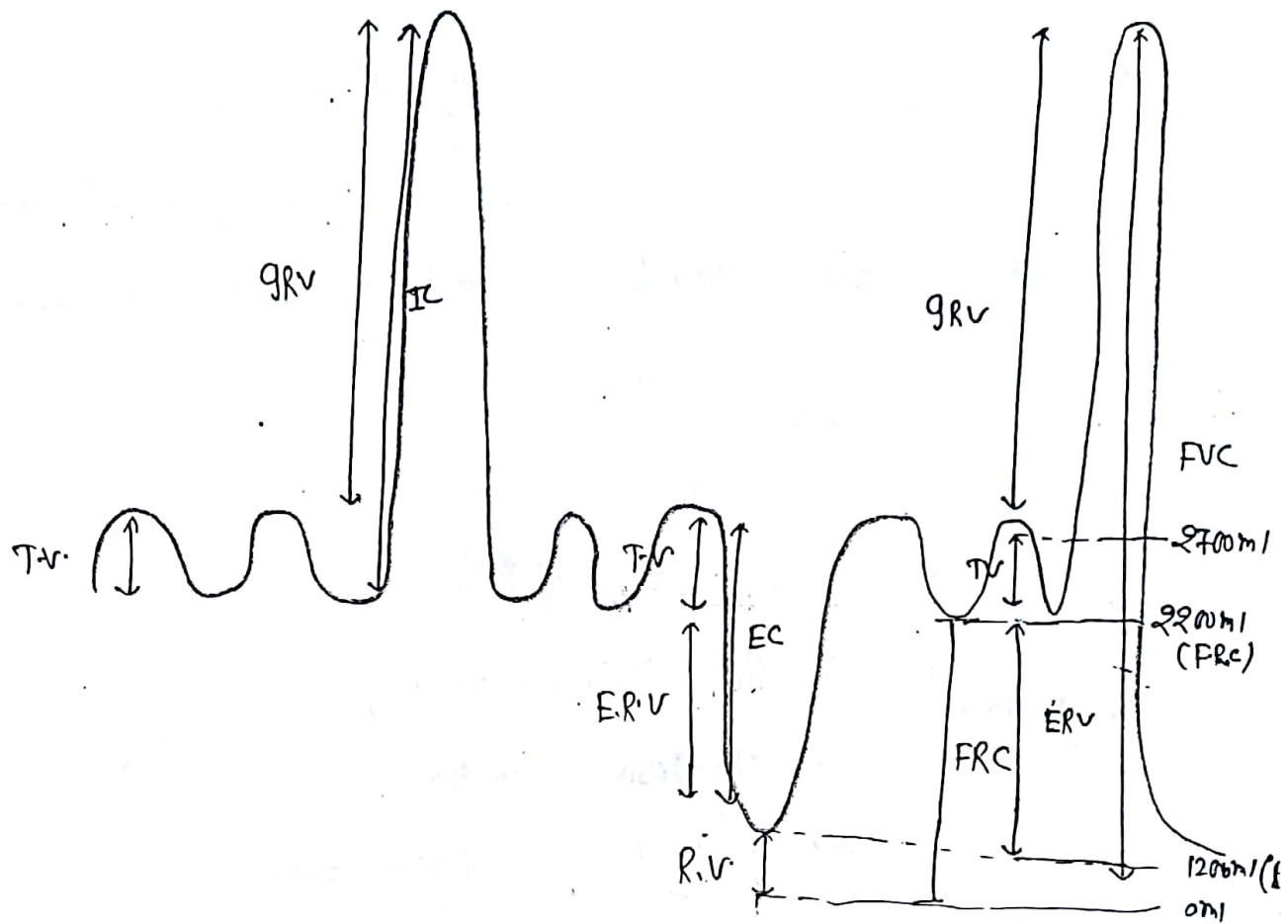
- 1100 ml = ♀

Inspiratory Capacity \Rightarrow IRV + TV

Expiratory Capacity \Rightarrow ERV + TV

Functional Residual capacity \Rightarrow Volume of Air \oplus in Lung @ the end of
(N) expiration

\hookrightarrow ERV + RV ; (N) value = 1200 ml σ ; 1100 ml ♀



Forced vital capacity \Rightarrow Volume of Air expired forcefully after a forcefully Inspiration.



$$\boxed{\text{ERV} + \text{TV} + \text{GRV}}$$

Total Lung capacity = 6000ml; 4200g



$$\boxed{\text{GRV} + \text{TV} + \text{ERV} + \text{RV}}$$

* Lung volume @ Normal expiration \Rightarrow Functional Residual capacity (FRC)

* Lung volume @ the end of Forceful expiration \Rightarrow Residual volume (RV)

* Lung volume At the end of Forceful Inspiration
↳ Total Lung capacity

* volume of Air expired forcefully after a forceful inspiration
↳ Forced vital capacity

* Which volume can't be measured by Routine spirometry

RV
FRC
TLC } (X)

- For FRC \Rightarrow ERV + RV

Measurement
↓

i) He dilution technique

ii) N₂ washout Method

iii) Whole body plethysmography

↳ Most accurate
↳ also measure volume of air-trapped in Bullae

- For R.V. \Rightarrow RV = FRC - ERV
↳ Measure by Routine spirometry

Q N₂ Can be used in Measurement of

a) Anatomical dead space - Single Breath N₂ Analysis

b) FRC - by N₂ washout Method

c) Both

TIMED VITAL CAPACITY

FEV₁

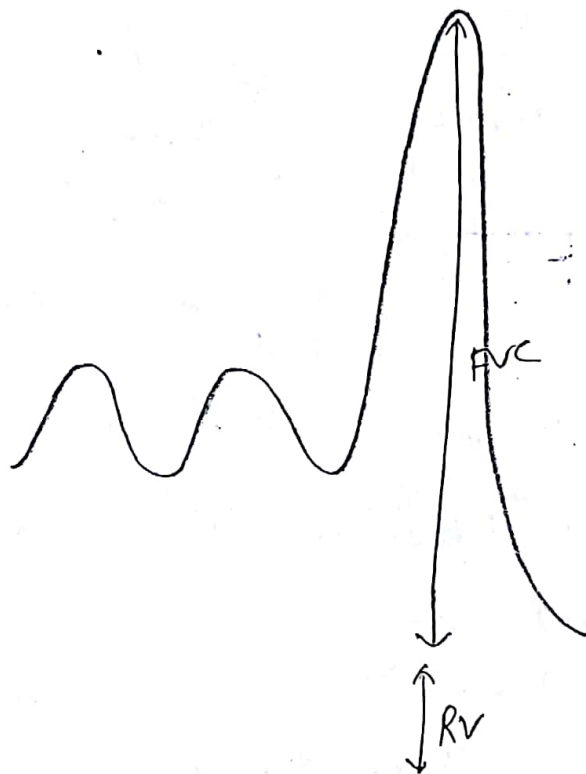
FEV₂

FEV₃

Forcefully expired
volume of Air @
the end of 1 sec

@ 2 sec

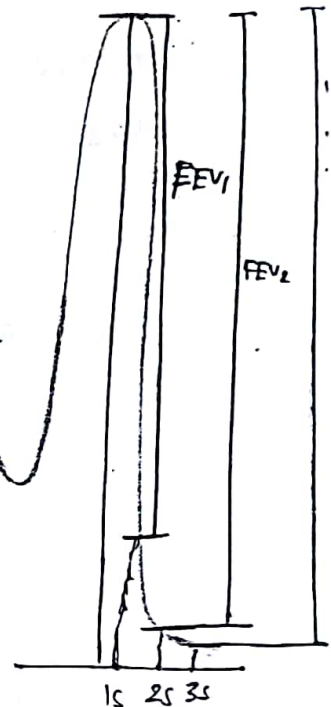
@ 3 sec



$$\frac{FEV_1}{FVC} = \frac{0.7}{0.8} = 70-80\%$$

$$\frac{FEV_2}{FVC} = \frac{0.9}{1.0} = 90\%$$

$$\frac{FEV_3}{FVC} = \frac{0.97}{1.0} = 97-98\%$$



Obstructive Lung Disease

$$\frac{FEV_1 \downarrow \downarrow}{FVC \downarrow} \quad \downarrow -$$

Restrictive Lung Disease

$$\frac{\downarrow FEV_1}{\downarrow \downarrow FVC} \quad \textcircled{N} \text{ or } \uparrow$$

VENTILATION

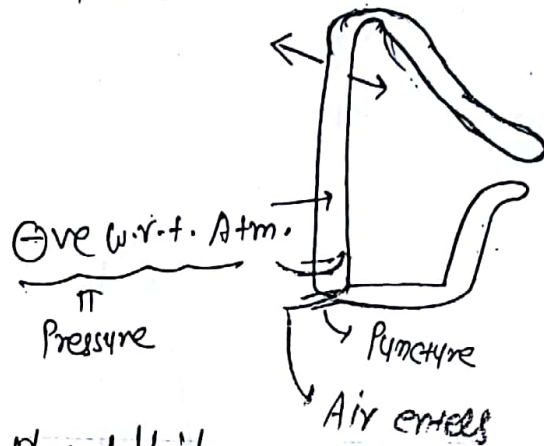
INTRAPLEURAL PRESSURE / PLEURAL PRESSURE / INTRATHORACIC PRESSURE /
ESOPHAGEAL PRESSURE \rightarrow

i) Lung Recoil & chest wall Recoil



Two opposing forces

\hookrightarrow g+ creates
+ve pressure in pleural
space



ii) continuous drainage of pleural fluid
into the lymphatics.

\Downarrow
Zero Pressure w.r.t. Atm.

In Emphysema

\hookrightarrow \uparrow ~~lung~~ ^{chest} Recoil force (Lung Recoil force less)
b/c of destruction of
elastic fibres of
Lungs

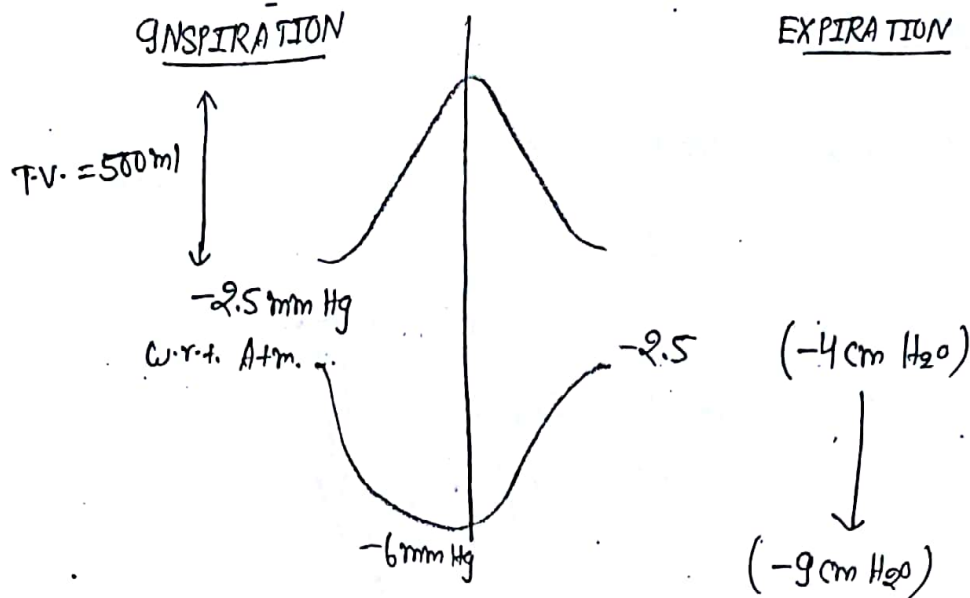


Barrel shaped

At FRC

\hookrightarrow Lung Recoil = Chest wall Recoil
 \hookrightarrow so, it is k/as "Relaxation volume of Lungs"

* What happen to Intrapleural pressure \bar{c} Respiration \rightarrow



Pleural pressure May \oplus ve during "VALSALVA" \rightarrow also during Labour

Straining (Forceful expiration against closed Glottis.)
 Any kind of straining is valsalva

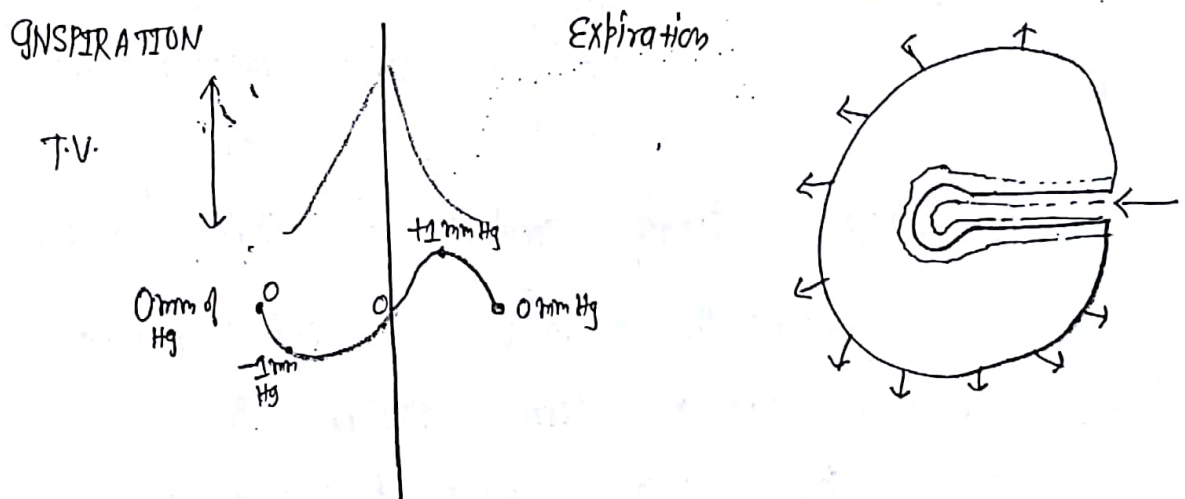
In Forcefully expiration

\rightarrow Pressure goes to -10 mm Hg



- * During valsalva \Rightarrow \downarrow venous Return
- \downarrow Blood Pressure
- \downarrow cardiac output

II. INTRAPULMONARY PRESSURE / AIRWAY PRESSURE / ALVEOLAR PRESSURE \rightarrow



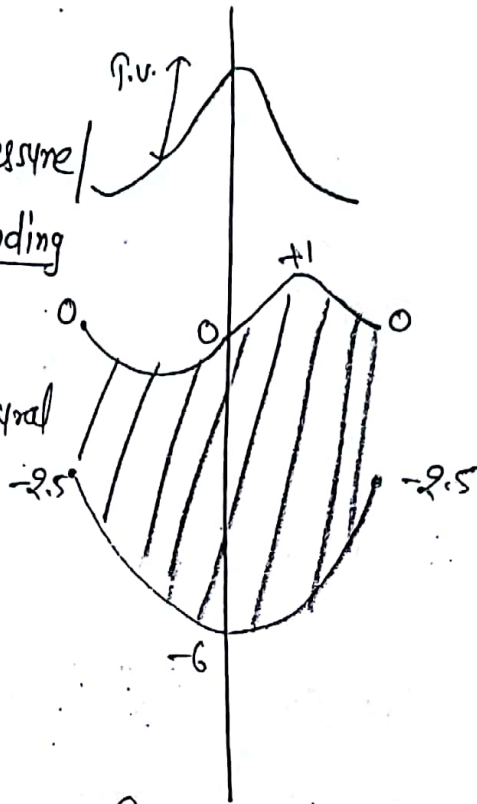
NET Pressure \Rightarrow

Kla " Transpulmonary Pressure /

Transmural Pressure / Distending

Pressure "

\Rightarrow Intrapulmonary - Intrapleural
(P) (P)



Qa Transpulmonary Pressure @ start of Inspiration

$$\hookrightarrow 0 - (-2.5) = +2.5 \text{ mm of Hg}$$

Qa Transpulmonary Pressure @ ~~start~~ end of Inspiration

$$\hookrightarrow 0 - (-6) = +6 \text{ mm of Hg}$$

LUNG COMPLIANCE

Compliance \Rightarrow Distensibility

$$\Rightarrow \boxed{C = \frac{\Delta V}{\Delta P}}$$

$\Delta V =$ change in volume

$\Delta P =$ change in transpulmonary pressure

(N) value of Lung compliance $\Rightarrow 0.2 \text{ L / cm H}_2\text{O}$

Lung + chest wall compliance $\Rightarrow 0.1 \text{ L / cm H}_2\text{O}$

Q: Change in Lung volume = 600ml ; Esophageal pressure changes from -4 cm of H₂O @ start of Inspiration & -8 cm H₂O @ end of Inspiration ;

Lung compliance = 22

(160)

Transpulmonary Pressure: $\Rightarrow 0 - (-4) \Rightarrow +4$
 \downarrow
 $0 - (-8) \Rightarrow +8$
 $\Rightarrow \text{change } (+4)$

$$C = \frac{\Delta V}{\Delta P} = \frac{600 \text{ mL}}{4 \text{ cm H}_2\text{O}} = 150 \text{ mL/cm H}_2\text{O}$$

SPECIFIC COMPLIANCE

$$\frac{\text{Compliance}}{\text{FRC}} = \text{Specific Compliance}$$

In Emphysema \rightarrow \uparrow compliance (Lung)
 $\uparrow \uparrow$ FRC
 \hookrightarrow so, specific compliance \downarrow .

condⁿ in which compliance \uparrow & specific compliance \downarrow
 \hookrightarrow Emphysema

* Compliance $\propto \frac{1}{\text{Surface tension}}$; Surface tension $\propto \frac{1}{\text{Surfactant}}$

**

Compliance \propto Surfactant

SURFACTANT \Rightarrow Secreted by Type-II Pneumocytes
↳ Dipalmitoyl Phosphatidyl Choline

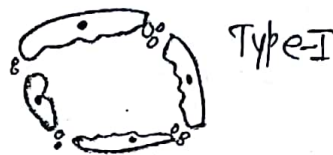
Q. Which is More Numerous \Rightarrow

Type-I \Rightarrow 40%

~~Type-II~~ \Rightarrow 60%

Q. Which are having More alveolar Surface Area \Rightarrow

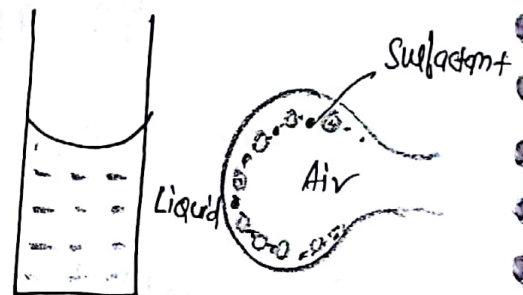
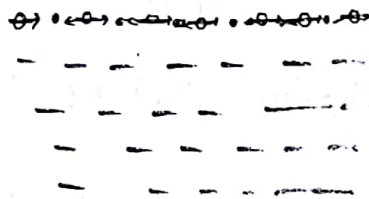
~~Type-I~~ \Rightarrow 95%
Type-II



* Surface tension \Rightarrow (a) Air-Liquid Interface

Air

Liquid



With expiration



↓
Less concn of Surfactant molecules
per Unit Area



↓↓ Surface tension

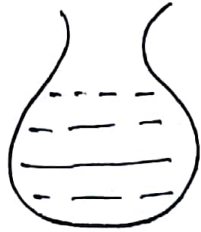


Helps to Maintain alveolar stability. QQ

99

Saline ventilated Lung

No Air-Liquid
Interface

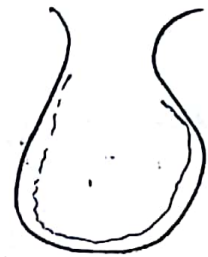


↓
Surface tension = 0

↓
↑ Compliance (Better Compliance)

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Air ventilated Lung



Air-Liquid Interface

↓
Surface tension $\Rightarrow \oplus$

↓
↓ Compliance as compared to
Saline ventilated Lung.

* Hormones which affect Surfactant \Rightarrow

i) Thyroid \Rightarrow ↑ type II ^{Pneumocyte} activity

So; In Hypothyroidism \Rightarrow RDS May seen in Newborn

ii) Insulin \Rightarrow ↓ type II Pneumocyte activity

↳ So; Babies born to Diabetic Mother \rightarrow More Likely to
Suffer from RDS.

iii) Glucocorticoids \Rightarrow ↑ type II Pneumocyte Maturation

↳ In pre-term babies \Rightarrow Give Steroids

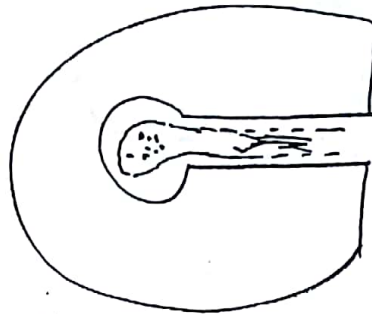
DYNAMIC COMPRESSION OF AIRWAYS

During Forcefully expiration



Tendency of Airways to collapse

↳ k/a "dynamic compression of Airways".



In Early Bronchial Asthma \Rightarrow Expiratory wheeze \oplus

At end of Forceful expiration



Airway collapse is complete



Air is trapped in Alveoli

↳ This Air is k/a "Residual volume"



this is d/t "dynamic compression of Airways".

WORK DONE IN QUIET BREATHING

\Rightarrow 0.3 - 0.8 Kg-m/min

65% (2/3rd)

35%

against elastic forces

against Resistive forces

43%

22%

against surface tension elasticity

against tissue elasticity

28%

7%

against Airway Resistance

against viscous Resistance

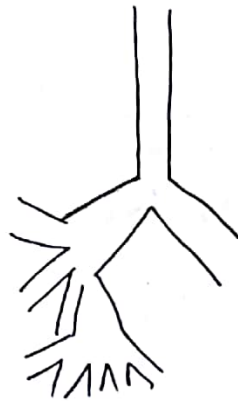
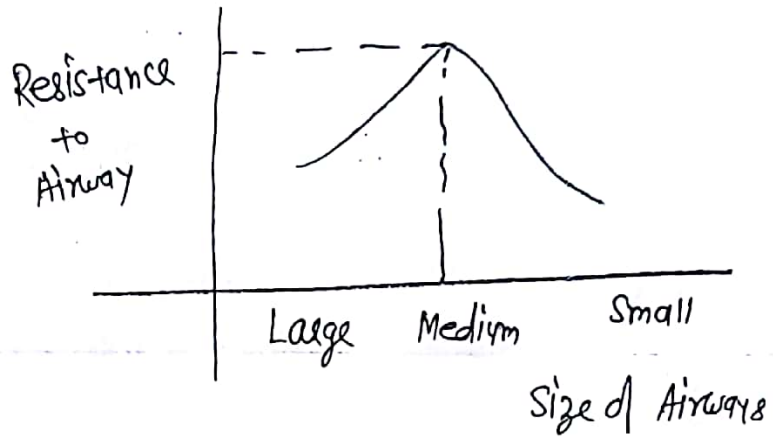
Q. Which Airways have Max^m Resistance to Airflow? 102

(a) Large sized Airways

~~(b) Medium sized Airways~~

(c) Small

$$R \propto \frac{1}{r^4}$$



WEIBEL'S CLASSIFICATION OF TRACHEOBRONCHIAL TREE :-

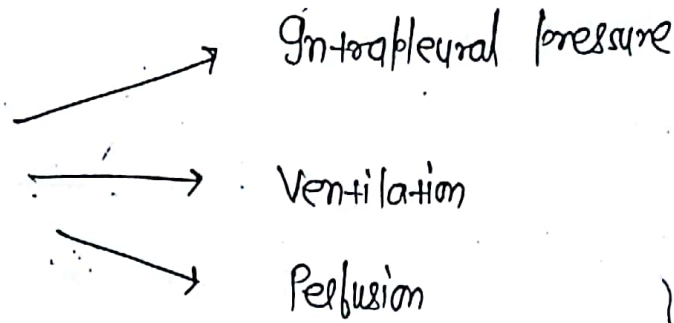
- * 23 Generation
- * Trachea \Rightarrow Generation 0
- * 1-16 \Rightarrow Conducting zone
- * 17-23 \Rightarrow Respiratory zone

Medium size Airways = 3rd - 5th Generation

	Medium size Airways	Small size Airways
Total cross sectional Area	↓	↑
velocity of Airflow	↑	↓
Reynold's No. $(R = \frac{\rho v d}{\eta})$	↑	↓
	Turbulent Airflow ⊕ ↳ d ^l + i ^t Resistance of Airflow res in it.	

VENTILATION PERFUSION GRADIENT IN ERECT POSTURE

BAO
Base to Apex
there is Decrease
in



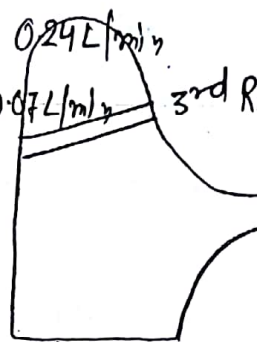
But $\frac{V}{Q}$ Ratio \Rightarrow \uparrow es from Base to Apex.

$$\frac{V}{Q} = 3.3$$

$$\text{Ventilation} = 0.24 \text{ L/min}$$

$$\text{Perfusion} = 0.07 \text{ L/min}$$

$$\frac{V}{Q} = 1$$



$$\frac{V}{Q} = 0.63$$

$$\text{Ventilation} = 0.82 \text{ L/min}$$

$$\text{Perfusion} = 1.29 \text{ L/min}$$

Avg. V/Q Ratio @ Lung $\Rightarrow 0.8$

Q. P_{aO_2} is Max^m at \Rightarrow a) Base; $\Rightarrow \frac{V}{Q} < 1.0$
b) ~~Apex.~~

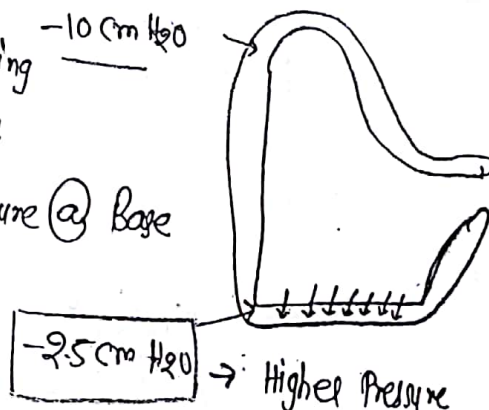
\hookrightarrow Incomplete oxygenation

* Base to apex Intrapleural Pressure \downarrow es \Rightarrow

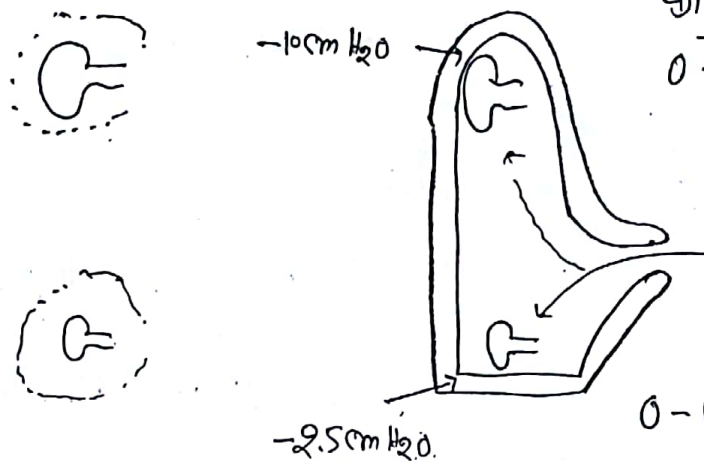
Probable Reason \Rightarrow During Standing

Weight of Lungs acts as Base

\hookrightarrow \uparrow es Pleural pressure @ Base



* Base to Apex ves in Ventilation \Rightarrow



Distending Pressure

$$0 - (-10) = +10 \text{ cm H}_2\text{O}$$

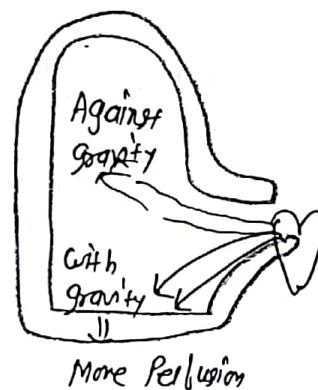
$$0 - (-2.5) = +2.5 \text{ cm H}_2\text{O}$$

Q. Ventilation is More in alveoli @ Base??

a) Alveoli @ Base have More Surfactant;

b) Alveoli @ Base are More compliant

* Base to Apex ves in Perfusion \Rightarrow

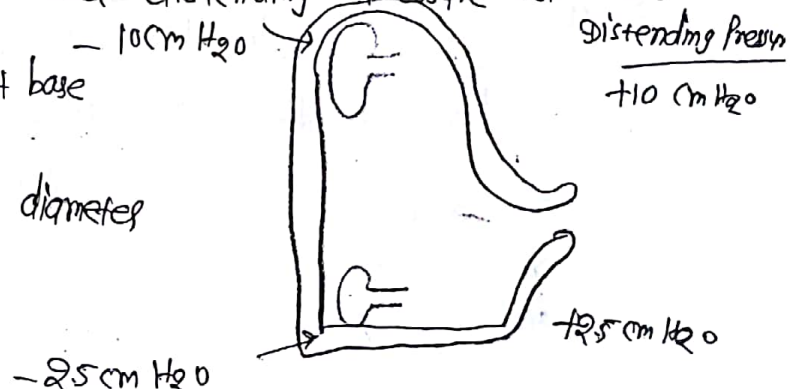


CLOSING VOLUME

- It is the Lung volume at which Airways at base begins to collapse; b/c of Lesser distending Pressure at base

Distending Pressure is less at base

therefore; Airway & Alveolar diameter is less at base



* closing volume > Residual volume

↳ b/c it is not expired volume; it is Lung volume

**

FRC > closing volume > Residual volume

FRC > Closing volume > Residual volume

* Elastic fibres \Rightarrow Exert Radial traction on Airways



Keep the Airways Patent

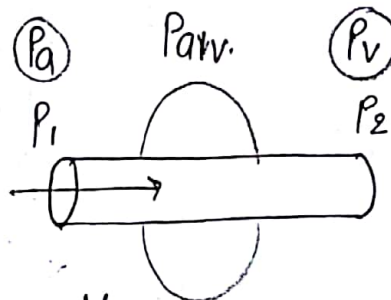
* With Age \Rightarrow ↓ Lung elastic fibres

Mid 70's \Rightarrow Huge Reduction (↓↓) Lung elastic fibres

↳ ↓ tendency of Airways to collapse

↓
closing volume approaches FRC.

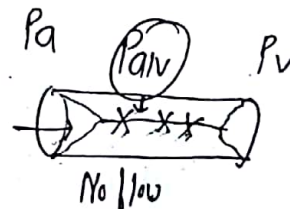
ZONES IN LUNG IN ERECT POSTURE



ZONE 1 \rightarrow Zone of No flow

Parvolar > Pa > Pv

↓
No Zone 1 in (N) Lung



Zone 1 prev. at Apex in Hypertension; Hemorrhage; Over Pressure ventilation

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Zone 2 \Rightarrow Zone of Intermittent Flow/Pulsatile flow. \rightarrow Klaw "care of av effect"

During Systole $\Rightarrow P_a > P_v > P_{Aiv} \Rightarrow$ Flow \oplus

During Diastole $\Rightarrow P_a > P_{Aiv} > P_v \Rightarrow$ Flows stop

\rightarrow prt. at Apex.

Zone 3 \Rightarrow Zone of continuous flow

$P_a > P_v > P_{Aiv}$

$\rightarrow \oplus \otimes$ Base of Lung
@ Base of lung

PARTIAL PRESSURES

INSPIRATION

f. of $O_2 \Rightarrow 21\%$

EXPIRATION

16%

QA Mouth - to - Mouth Respiration

At sea level ; Atm. Pressure = 760 mm of Hg

$$P_{O_2} = \frac{21}{100} \times P_B = \frac{21}{100} \times 760 = 160 \text{ mm of Hg}$$

QA At High Altitude \rightarrow ~~(a) P_B (Barometric Pressure)~~

$P_{O_2} = \frac{21}{100} \times 500$ (if veg to 500 (atm. Pressure))

$= 105 \text{ mm of Hg.}$

(b) \downarrow f. of O_2

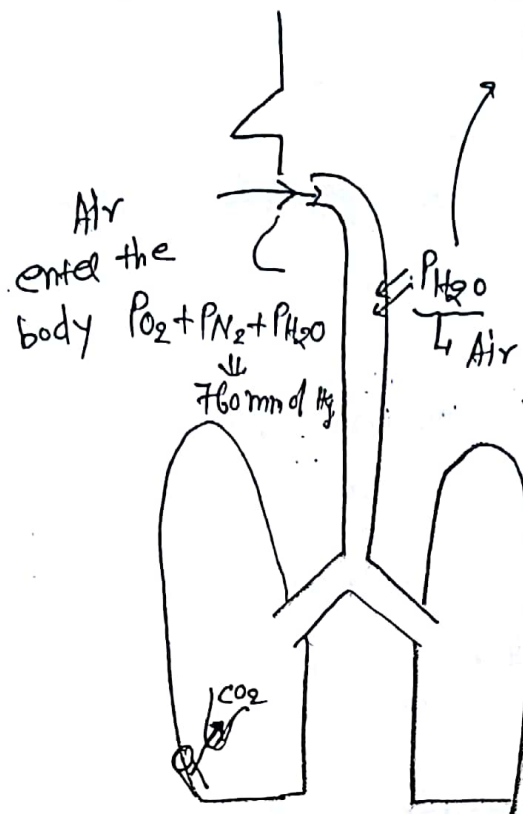
(c) Both

(d) None

$$P_{O_2} + P_{N_2} = 760 \text{ mm of Hg}$$

H_2O vapour comes from epithelial cells.

$P_{H_2O} = 47 \text{ mm of Hg}$
(respective to altitude & Environmental temp.)

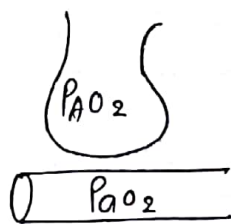


Alveolar Partial Pressure of oxygen
($P_{A O_2}$)
⇒ By Alveolar Gas equation

Alveolar O_2 ⇒
provided

$$\hookrightarrow \frac{V}{Q} \geq 1.0$$

li> Respiratory Memb. ⇒ (N)



HENRY'S LAW

Partial Pressure in the solution is equal to partial pressure above the solution.

* Alveolar Gas equation ⇒

$$P_{A O_2} = \left[(P_B - P_{H_2O}) \times \frac{\text{fraction concn of } O_2}{R} \right] - \frac{P_{A CO_2}}{R}$$

\downarrow
 $P_{I O_2}$

R = Respiratory Quotient

$$R.Q. = \frac{\text{Volume of } CO_2 \text{ Produced}}{\text{Volume of } O_2 \text{ Consumed}}$$

for Carbohydrate = 1
for Mixed diet = 0.8

$$P_{AO_2} = \left[(P_B - P_{H_2O}) \times \frac{\text{fractional concn of } O_2}{100} \right] - \frac{P_{ACO_2}}{R}$$

At Sea level

$$P_{AO_2} = \left[(760 - 47) \times \frac{21}{100} \right] - \frac{40}{0.8}$$

$$\Rightarrow P_{AO_2} = 105 \text{ mm Hg}$$

Q. How Much is P_{AO_2} if he receives 4 times Atmospheric pressure & 100% O_2 .

Hyperbaric O_2 chamber

$$4 \times 760 = 3040$$

$$P_{AO_2} = \left(3040 - 47 \right) \times \frac{100}{100} - \frac{40}{0.8}$$

$$\approx 3,000 \text{ mm Hg}$$

given in
Gram -ve septicemia
 CO_2 Poisoning

RESPIRATORY EXCHANGE

Arterial Blood

Venous Blood

Total O_2
(mL/dL)

19 mL/dL

14 mL/dL

P_{O_2} (mm of Hg)
(dissolved O_2)





95 mm of Hg






40 mm of Hg

SO_2 (%)

97-98%

75%

 O_2
 O_2
 O_2
 O_2

 O_2
 O_2
 O_2
 O_2
 O_2

Arterial Blood

Venous blood

Total CO_2
(mL/dL)

49 mL/dL

53 mL/dL

PCO_2 (mm Hg)

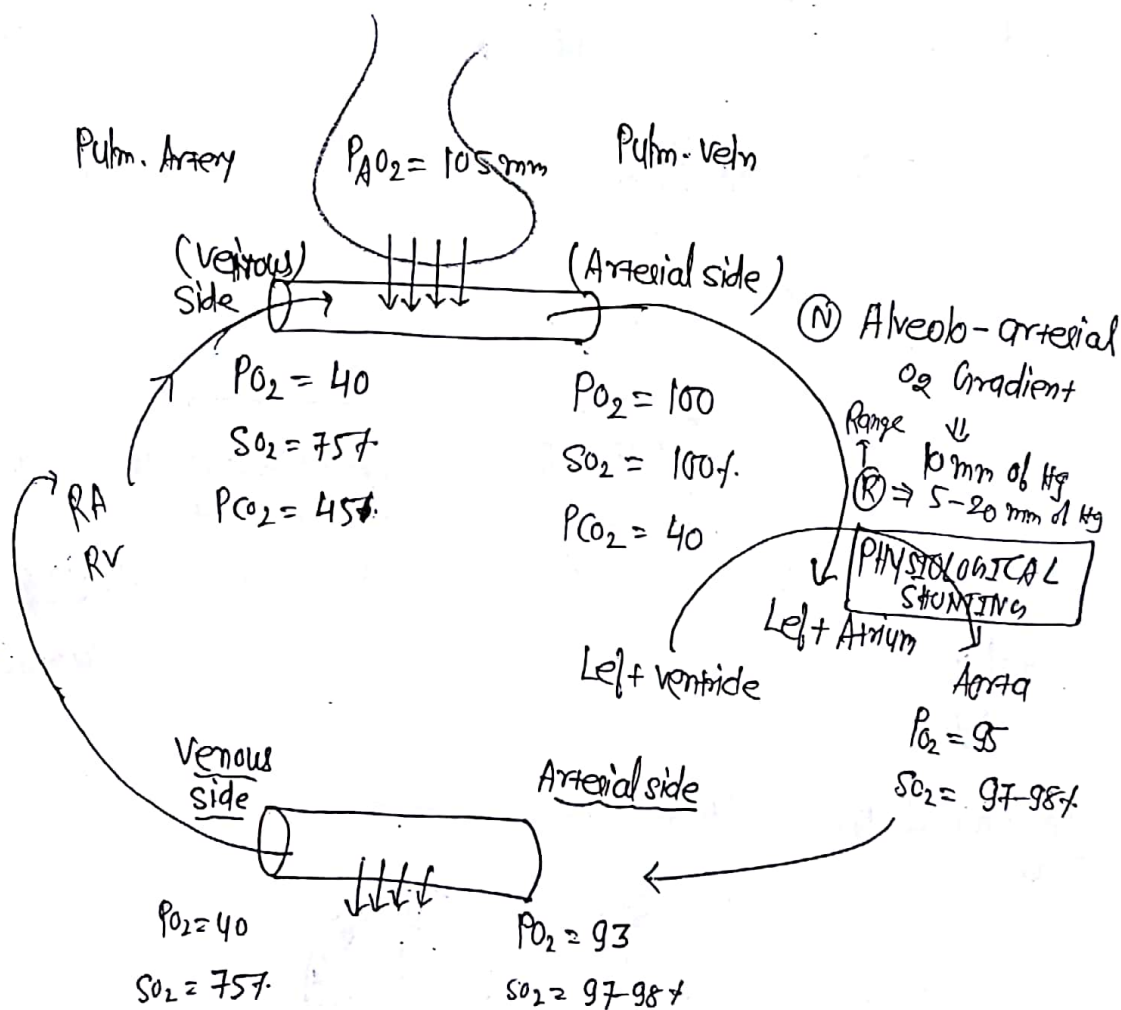
40

45

O_2 consumption at Rest \Rightarrow 250 mL/min

CO_2 production at Rest \Rightarrow 200 mL/min

$$R.Q. = \frac{\text{CO}_2 \text{ Produced}}{\text{O}_2 \text{ consumed}} = \frac{200 \text{ mL/min}}{250 \text{ mL/min}} = 0.8$$



- Q) Alveolo-arterial gradient is less in all except \Rightarrow
- (a) $R \rightarrow L$ Shunt;
 - (b) Pulmonary fibrosis
 - (c) Pulmonary edema;
 - ~~(d) High altitude \Rightarrow b/c exchange is not affected;~~
 \hookrightarrow as much as Alveolar $P_{A_{O_2}}$ less; arterial $P_{a_{O_2}}$ also less; so gradient same.

Pulmonary capillary Transient time (Blood stay in pulmonary capillaries)
 \hookrightarrow 0.75 - 0.85 sec

Tissue capillary Transient time (Blood stay in tissue capillaries)
 \hookrightarrow 1-2 sec

Qa Large change in $P_{O_2} \Rightarrow$ ~~a) pulmonary capillaries~~
 b) Tissue capillaries

Qa Largest Arterio-venous O_2 difference
 \hookrightarrow Heart

	$P_{a_{O_2}}$	$P_{v_{O_2}}$
Normal \Rightarrow	95	40
(a) coronary	95	20

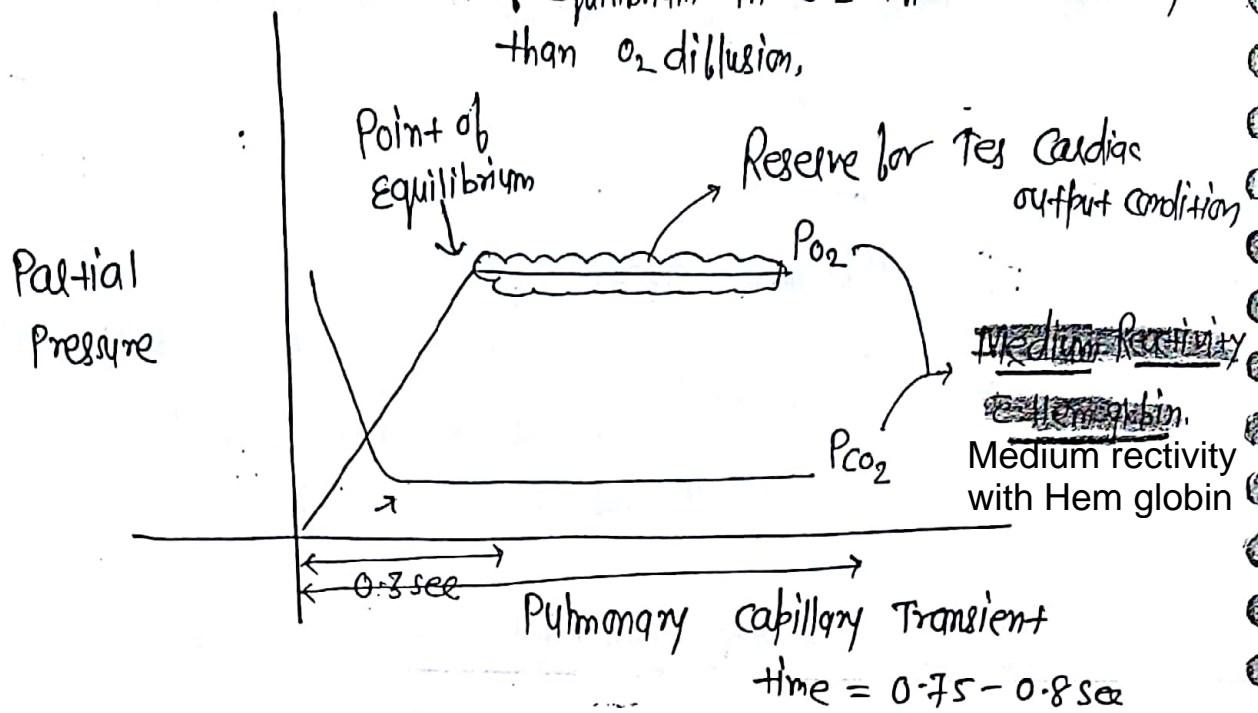
Qa Min^m Arterio-venous O_2 difference Renal blood flow = 1100-1200 ml/min
 \hookrightarrow 22-23% of CO

	$P_{a_{O_2}}$	$P_{v_{O_2}}$
\hookrightarrow Kidney	95	40
Kidney	95	70

Blood supply to the kidney is in excess of its Metabolic Need.

*

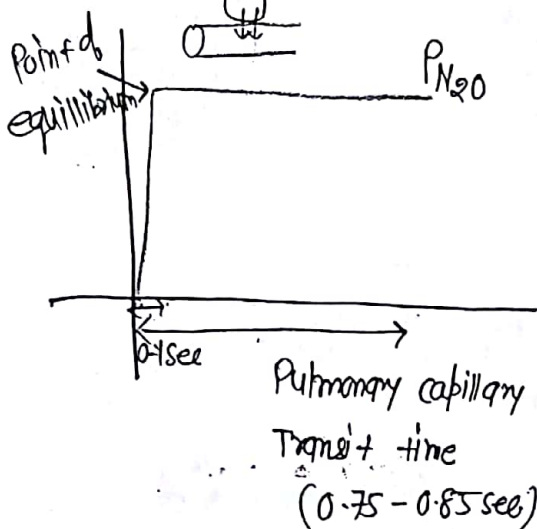
Point of equilibrium in CO_2 diffusion comes early than O_2 diffusion,



*

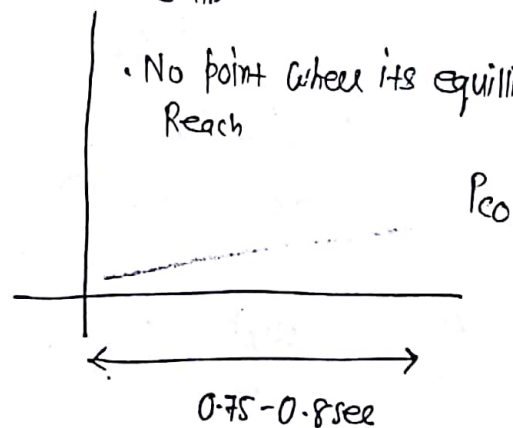
PERFUSION OF FLOW LIMITED GASES

- N_2O
- Gas which completes diffusion within pulmonary capillary transit time
- Nil transit time Reactivity with Hb



PERFUSION OF DIFFUSION LIMITED GASES

- CO
- Gas which doesn't equilibrate within pulmonary capillary transit time
- CO has very very high Reactivity \bar{c} Hb.
- No point where its equilibrium Reach



Q9) Which of the following is Diffusion Limited gas?

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(a) N_2O

(b) O_2

(c) CO_2

(d) CO

Perfusion or Flow Limited gas

OXYGEN TRANSPORT

(1) With Hb (As Oxy Hemoglobin)

Arterial blood

Venous blood

18.71 mL/dL

13.88 mL/dL

(2) As dissolved O_2 (95×0.003) 0.29 mL/dL

(40×0.003)
0.12 mL/dL

Total O_2 = 19 mL/dL

14 mL/dL

* O_2 content (mL/dL) = (O_2 in combination with Hb) + (Dissolved oxygen)

$$= \left(Hb (gm/dl) \times 1.34 + \% \text{ Saturation} \right) + \left(\frac{\text{Dissolved oxygen}}{(P_{O_2} \times 0.003)} \right)$$

(1 gm of Hb can transport 1.34 mL of O_2)


In Anemia \Rightarrow a) \downarrow Hemoglobin (Fe deficiency Anemia, Hemolytic Anemia)


b) \downarrow Saturation of O_2 (Carbon Monoxide poisoning, Methemoglobinemia)


 CO


 O_2


 O_2

 O_2

 $Fe^{3+} \times$

 $Fe^{3+} \times$

 O_2

 O_2

DISSOLVED OXYGEN



P_{O_2} (mm of Hg)



ml/dL

Solubility of O_2 ⇒ 0.003 ml/dL/mm of Hg

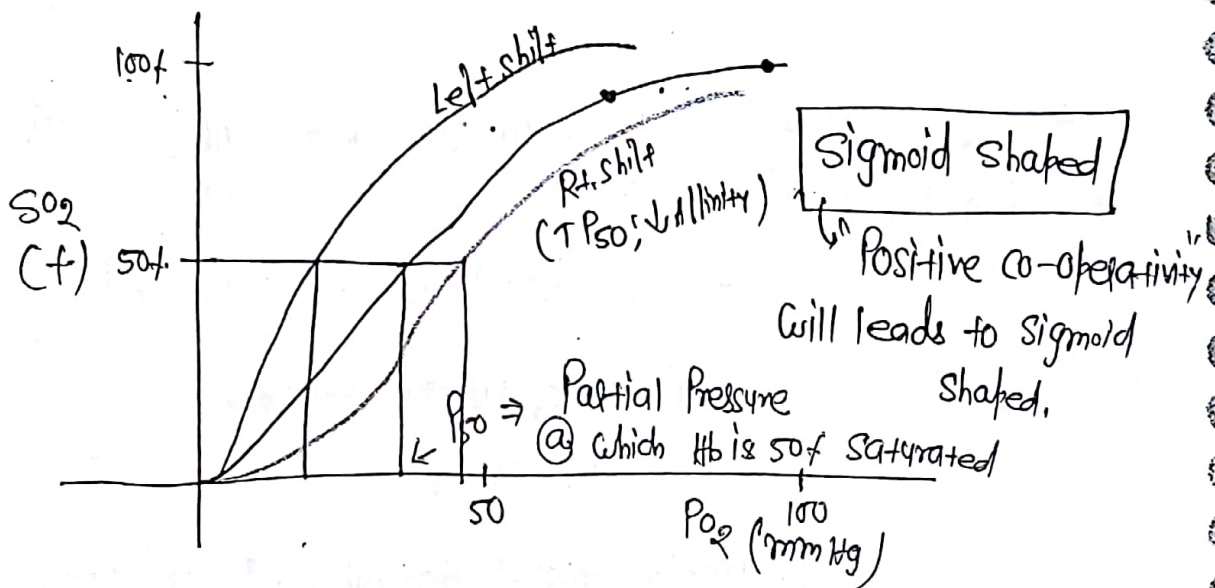
↳ if P_{O_2} is 1 mm of Hg ⇒ Dissolved O_2 is 0.003 ml/dL

So; if P_{O_2} is 100 mm of Hg ⇒ Dissolved O_2 is 0.3 ml/dL

if P_{O_2} is 90 mm of Hg ⇒ Dissolved O_2 is 0.27 ml/dL

if P_{O_2} is 80 mm of Hg ⇒ Dissolved O_2 is 0.24 ml/dL

* Oxygen Hb Dissociation curve ⇒



P_{O_2}	Saturation of O_2
95 mm of Hg	97-98%
60 mm of Hg	89%
40 mm of Hg	75%

Hypoxia → if P_{O_2} is less than 60 mm of Hg.

Deoxy Hb (Tense configuration) → oxy Hb (Relaxed configuration)

T → R conversion

T -----> R conversion

$P_{50} \Rightarrow$ Normally 25-27 mm of Hg
 $= 3.6 \text{ kPa}$

(108)
 $[1 \text{ kPa} = 7.5 \text{ mm of Hg}]$

Right shift of curve \Rightarrow

$\uparrow P_{50}$ (Favours delivery shift to Right)
 \downarrow Affinity

condⁿ \Rightarrow

$\uparrow P_{CO_2}$
 $\uparrow H^+$
 $\downarrow pH$
 $\uparrow 2,3-DPG$
 $\uparrow \text{temp.}$
 Hbs

caused by \rightarrow

G \rightarrow Growth Hormone
 E \rightarrow Exercise (Untrained Individual)
 T \rightarrow Thyroid (excess)
 A \rightarrow Anemia
 Altitude (high)
 Androgen

4 moles of O_2 binds \bar{c} 1 mole of Hb; but 1 mole of O_2 binds \bar{c} 1 mole of Hb; but both binds at same place

Left shift of curve \Rightarrow

$\downarrow P_{50}$ (Favours affinity shift to Left)
 \uparrow Affinity

condⁿ \Rightarrow

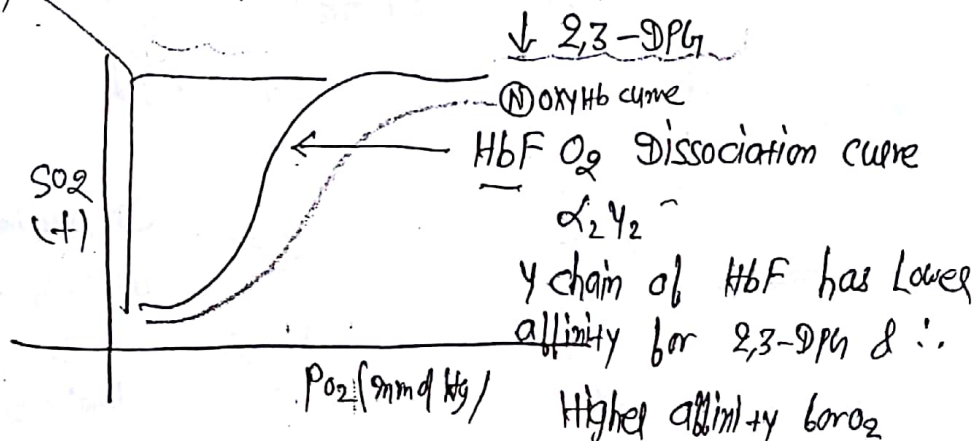
$\downarrow P_{CO_2}$
 $\downarrow H^+$
 $\uparrow pH$
 $\downarrow 2,3-DPG$
 $\downarrow \text{temp.}$
 HbF

1 mol of Myoglobin binds \bar{c} 1 mol of O_2

Myoglobin O_2 dissociation curve
 \downarrow
 Rectangular hyperbola
 $(P_{50} = 5 \text{ mm of Hg})$

HbF \Rightarrow

Myoglobin \Rightarrow Store house of oxygen in Muscles
 Banked blood \rightarrow Glycolysis



REGULATION OF RESPIRATION

NEURAL
CONTROL

CHEMICAL
CONTROL

(Chemoreceptors)

MEDULLA

→ Packmaker →

PRE BOTTZINGER COMPLEX

DRG

• Dorsal Respiratory Group

• "I" cells

• Function in (N); Quiet Respiration

DRG ("i" Neurons)

X

⊕ ↓

Phrenic N. Nucleus

X

(cervical spinal cord)



VRG

• Ventral Respiratory Group

• "I" & "E" cells

• Functions whenever Requirement rises (eg → Exercise)

DRG ("i")

X

⊕ ↓

X

⊕ ↓

Contraction
of diaphragm
⇓
Inspiration

Relaxation of
diaphragm
⇓
Expiration

DRG \rightarrow Inspiratory signal..

Receptor for Tidal Receptor \Rightarrow Muscle spindle of diaphragm
& ~~External~~ costal Muscle
Inter

*

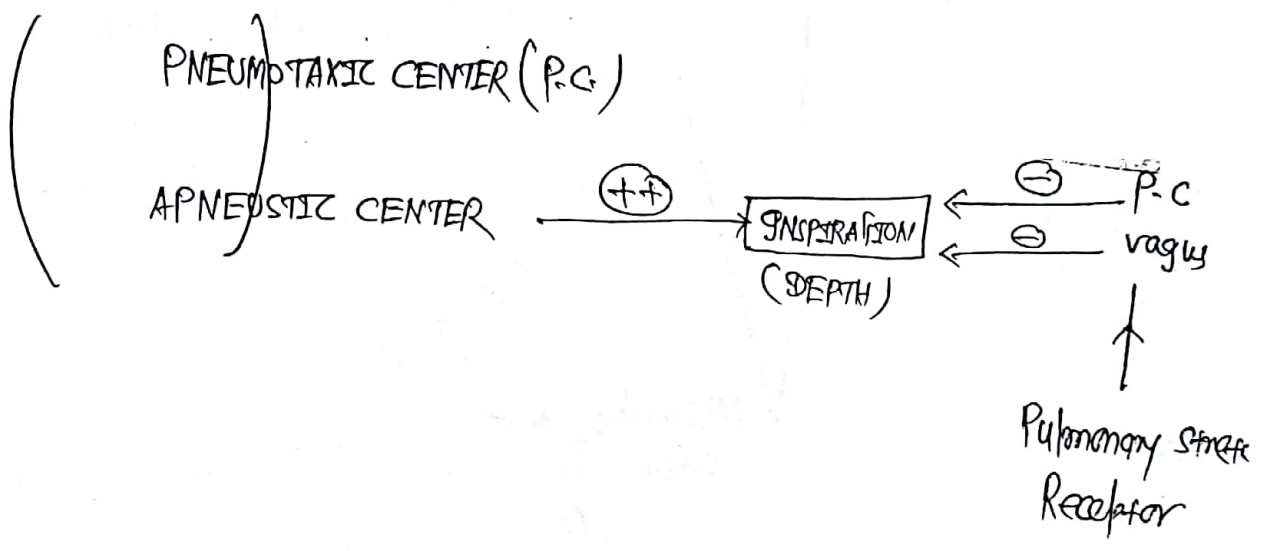
PONTINE
CENTERS



Smooth transition b/w Inspiration
& expiration



control depth of Inspiration



*

HIGHER CENTERS

\rightarrow Limbic system \Rightarrow Emotion & Respiration

\rightarrow Cerebral cortex \Rightarrow Voluntary control of Respiration

Q Vagal Stimulation

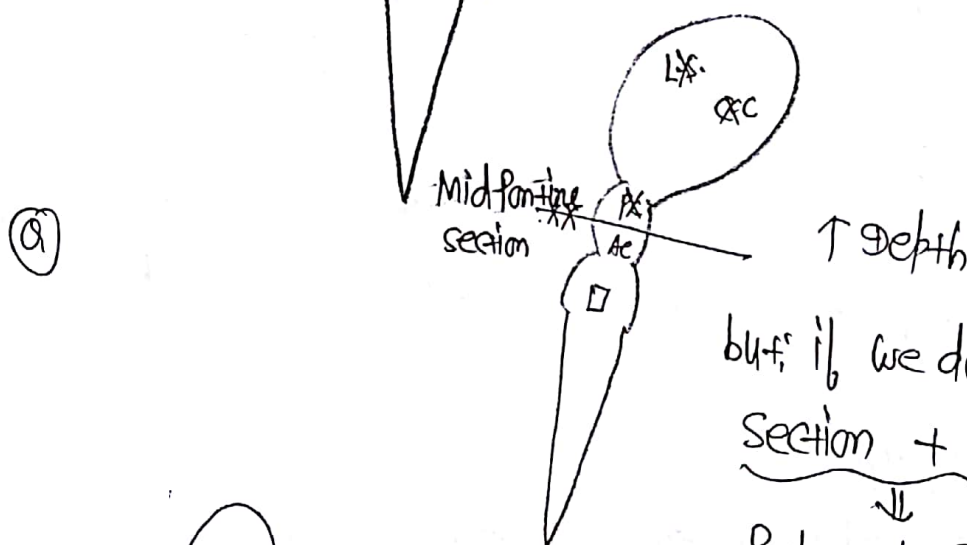
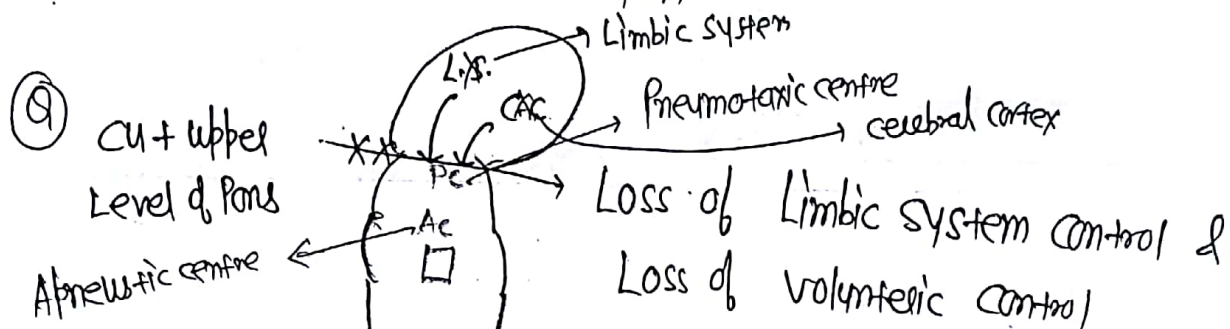
↳ ↓ Depth

Q Strong vagal stimulation

↳ Apnea

Q B/L Vagotomy

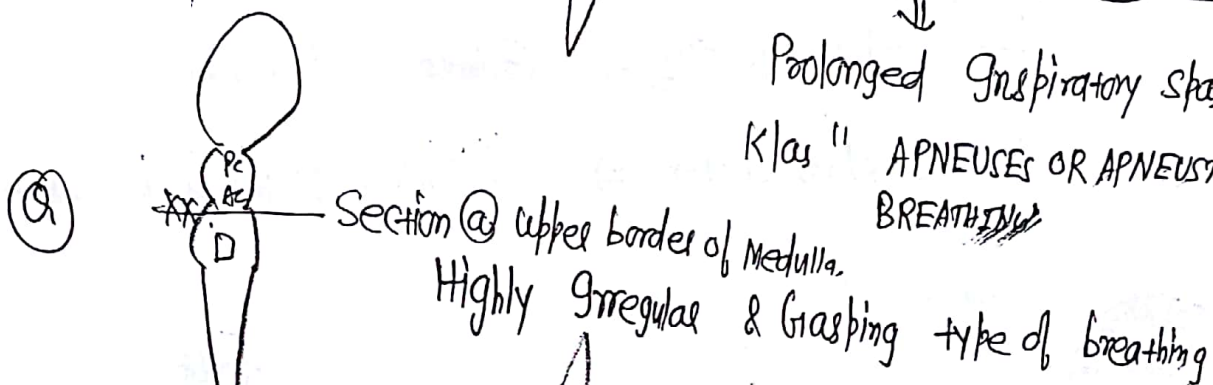
↳ ↑ Depth



but if we do Mid Pons section + B/L vagotomy both

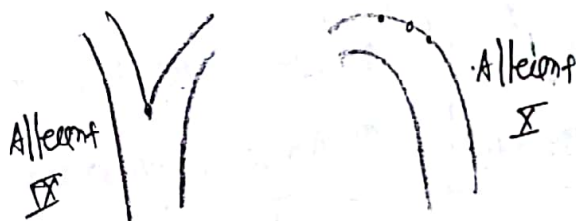
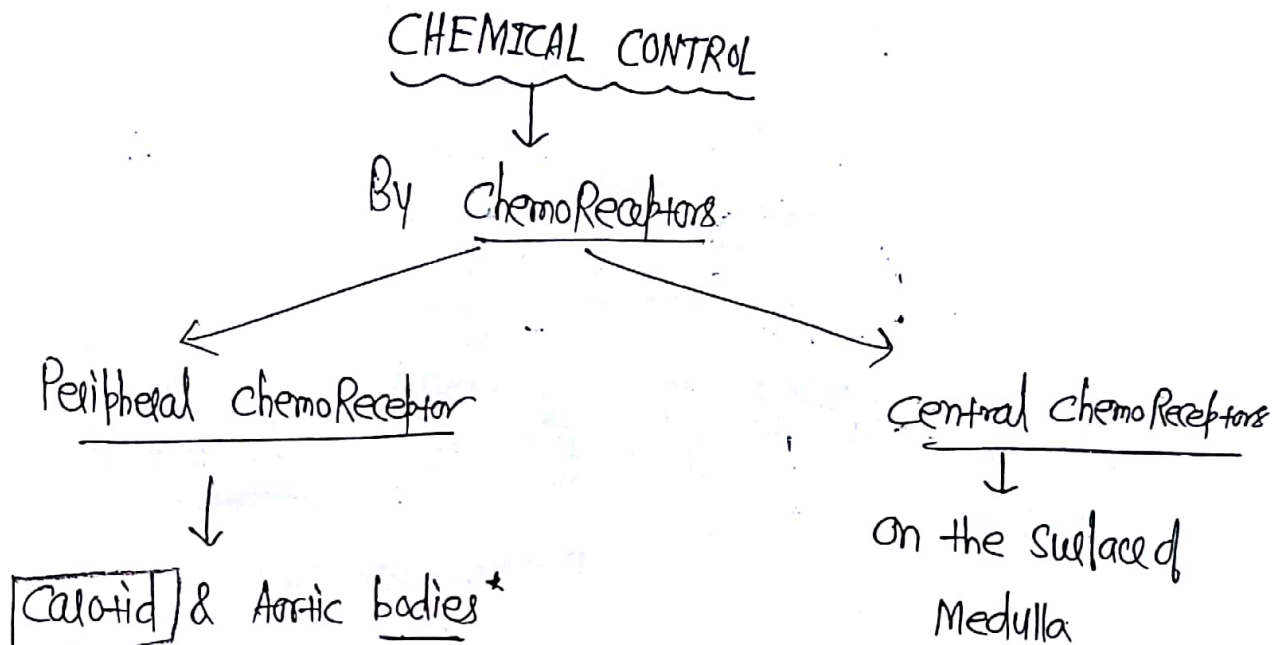
↓
Prolonged Inspiratory spasm

K/as " APNEUSIS OR APNEUSTIC BREATHING "



Q. Apnea will seen if section is at :-

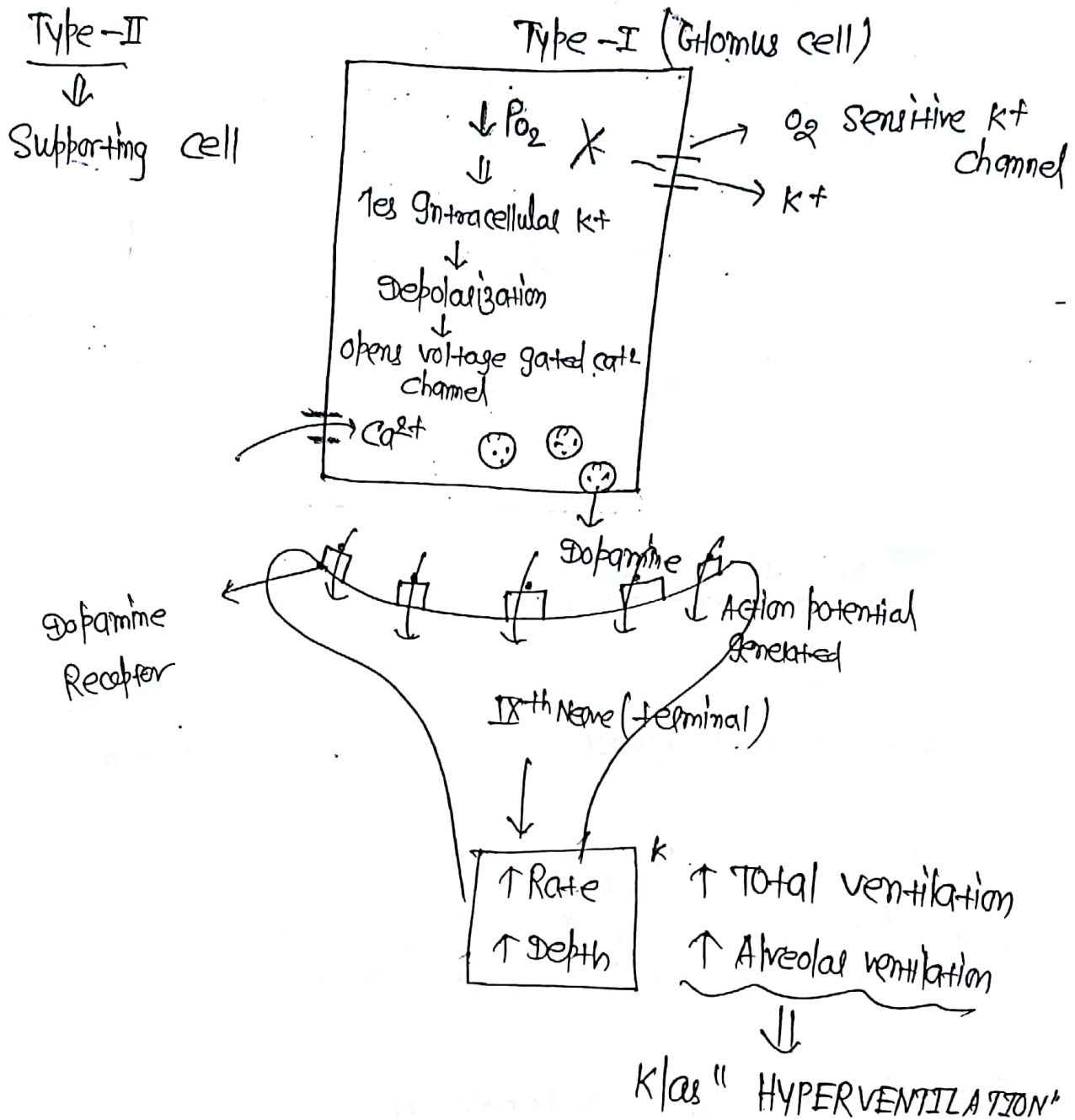
- (A) Upper Pons; (B) Lower Pons; (C) Upper Medulla;
(D) ~~Lower Medulla~~



Stimuli for Peripheral chemoreceptors ⇒

- | | |
|--|---|
| <p>i) $\downarrow P_{O_2}$ ← Most potent stimuli for Peripheral chemoreceptors</p> <p>ii) $\uparrow P_{CO_2}$</p> <p>iii) $\uparrow H^+$</p> <p>iv) $\downarrow PH$</p> <p>v) \uparrow Lactic acid</p> <p>vi) $\uparrow K^+$ (severe exercise)</p> <p>vii) severe cyanide</p> | <p>(A) Peripheral chemoreceptors stimulated by</p> <p>(a) $\uparrow P_{O_2}$</p> <p>(b) $\downarrow P_{CO_2}$</p> <p>(c) $\uparrow PH$</p> <p>(d) Cyanide poisoning</p> |
|--|---|

CAROTID BODY



CENTRAL MEDULLARY CHEMORECEPTORS (C.C.R)

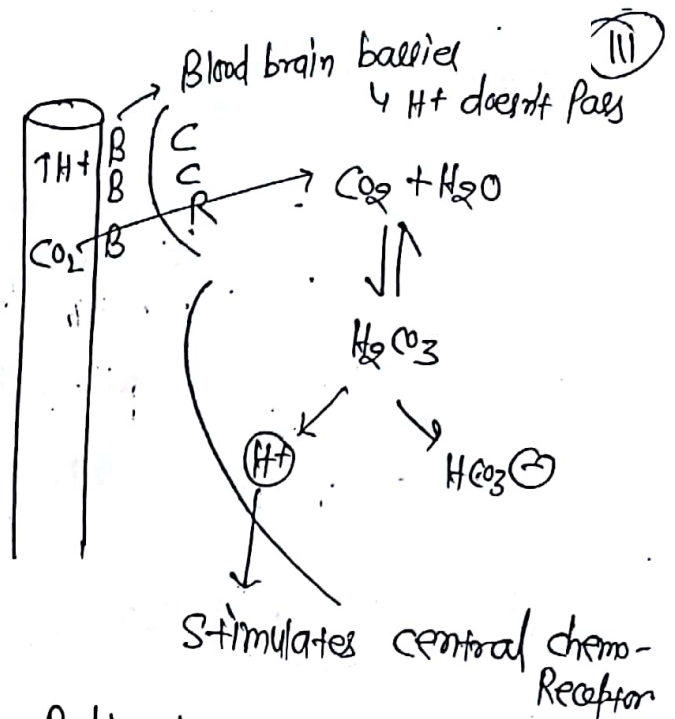
- ⑨ Most potent & direct stimulation for C.C.R
- \downarrow
- H^+

Q. Most potent stimulus for C.C.R. in blood \Rightarrow

(a) $\uparrow H^+$; (b) $\uparrow PCO_2$

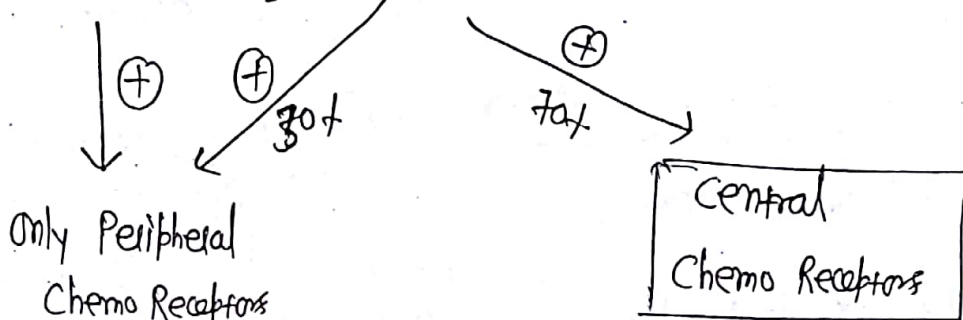
Q. Most potent stimulus for C.C.R. in CSF \Rightarrow

(a) $\uparrow H^+$; (b) $\uparrow PCO_2$



Q. Most potent stimulus for Respiration

(a) $\downarrow PO_2$; (b) $\uparrow PCO_2 \rightarrow$ Stimulate both



RESPIRATORY REFLEXES

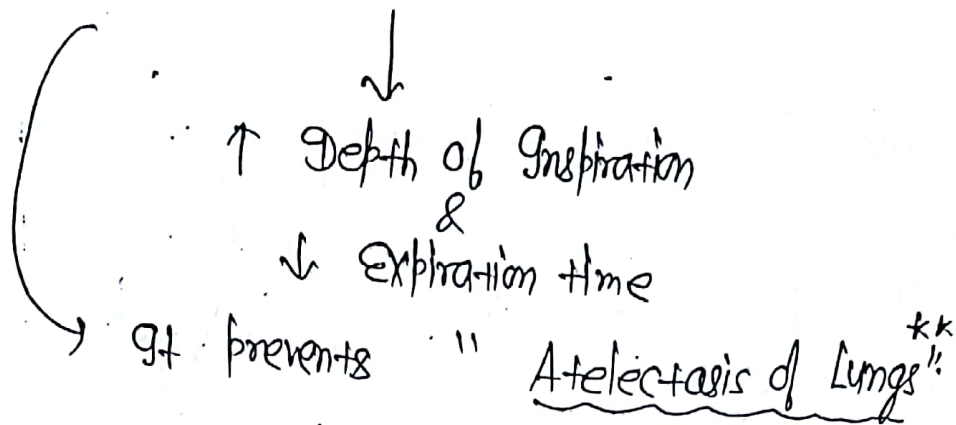
① HERING BREUR INFLATION REFLEX \Rightarrow

If Lung Inflation $\geq 1-1.5L \Rightarrow$ Stimulate Pulmonary stretch Receptors (+ @ Tracheo-bronchial tree)



\downarrow vagus
 \downarrow Depth & \uparrow Expiration time.

② HERING BREUR DEFLATION REFLEX !→



③ HEAD'S PARADOXICAL REFLEX !→

Inflation causes further Inflation of Lungs

Significance ⇒ Newborn's → 1st breath is d/t it

④ J-RECEPTOR REFLEX !→ J ⇒ Juxta-capillary

by Dr. A.S. PAINTAL

⊕ In Alveolo capillary Junction

Stimuli for J-Receptor ⇒ Hyperinflation

Pulmonary congestion

Pulmonary Edema

Pulmonary Embolism

Responses ⇒ Apnea (Transient) - Rapid Shallow ventilation

- Hypotension

- Bradycardia.

⑤ In Exercise → ↑ Rate; ↑ Depth
Which Receptor Stimulate ⇒ ① Pulmonary Stretch Receptor

In exercise (Mild to Moderate)

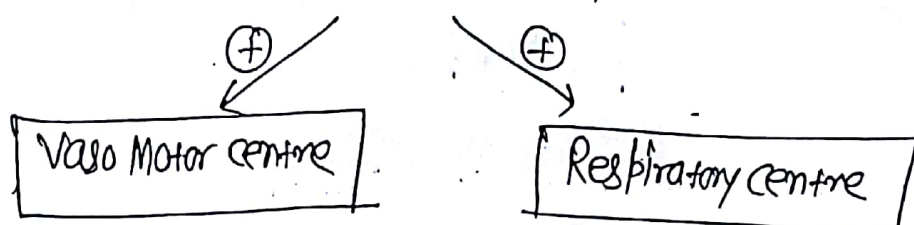
② J-Receptor

③ Chemoreceptor

~~④ Joint Proprioceptors~~

P_{O2} ↑
P_{O2} ↓
H⁺ ↑
↓
lim^{ts}

Joint - Proprioceptors



* but; In severe exercise: $\downarrow P_{O_2}$
 $\uparrow P_{CO_2}$
 $\uparrow H^+$
 $\downarrow K^+$ } \Rightarrow Joint Proprioceptors + Chemoreceptors both work

CYANOSIS — Bluish discoloration of skin & Mucosa

Deoxy Hb ≥ 4.0 gm/dL

So; Severe Anemia will Not pr. with cyanosis

While; In Polycythemia patient present \bar{c} cyanosis (maybe)

Meth Hb ≥ 1.5 gm/dL

Sulph Hb ≥ 0.5 gm/dL

HYPOXIA \Rightarrow O_2 deficiency at tissue level

1. **HYPOXIC HYPOXIA**

$\Rightarrow P_{O_2} < 60$ mm of Hg

$S_{O_2} < 89\%$

"M/c type of Hypoxia"

~~Cyanosis (+)~~

M/c type of Hypoxia
Cyanosis (+)

Causes \Rightarrow

~~High Altitude~~ High Altitude

~~Hypo Ventilation~~ Hypoventilation

~~Gulleian - Baare Syndrome~~ Gulleian - Baare synd

~~Bulbar Infarct~~ Bulbar infarct

~~Peripheral Chemoreceptor~~
Peripheral chemo-receptor
~~Stimulation~~
stimulation

\Rightarrow (+)

Anemic Hyoxia

either Hb Decrease or saturation of O₂

2. **ANEMIC HYPOXIA** \Rightarrow ~~either Hb decrease or saturation of~~ decrease

\downarrow
~~Cynosis = (-)~~
Cynosis - (-)

(Hb) \rightarrow \downarrow

(S_{O₂}) \rightarrow \downarrow

P_{O₂} \rightarrow (N) (b/c there is no problem regarding the exchange of O₂ here)

~~Peripheral Chemoreceptor~~
Stimulation

\Rightarrow (-)

eg \Rightarrow Meth Hb
CO Poisoning

3. **STAGNANT HYPOXIA** \Rightarrow

Stagnant hypoxia

~~Peripheral chemo-Receptor~~
(2-3gm)

\Rightarrow 1st Arterio-Venous O₂ difference
b/c of Sluggish blood flow

eg: CHF or circulatory shock
 \Rightarrow Very very very high rate of blood flow
 \Rightarrow 2000 mL/min/100gm

In Brain \Rightarrow 52 mL/min/100 gm

if there is less in blood flow rate

\rightarrow \downarrow Total volume of blood & therefore O₂ delivered to peripheral chemo receptors

④ **HISTOTOXIC HYPOXIA** \Rightarrow \downarrow Arterio-venous O_2 difference

~~eg \Rightarrow cyanide poisoning~~ Cyanide Posining

~~Peripheral chemoreceptor \rightarrow stimulation~~

Stimulation \rightarrow Min^m time Required
ACCLIMATIZATION * 4-5 days

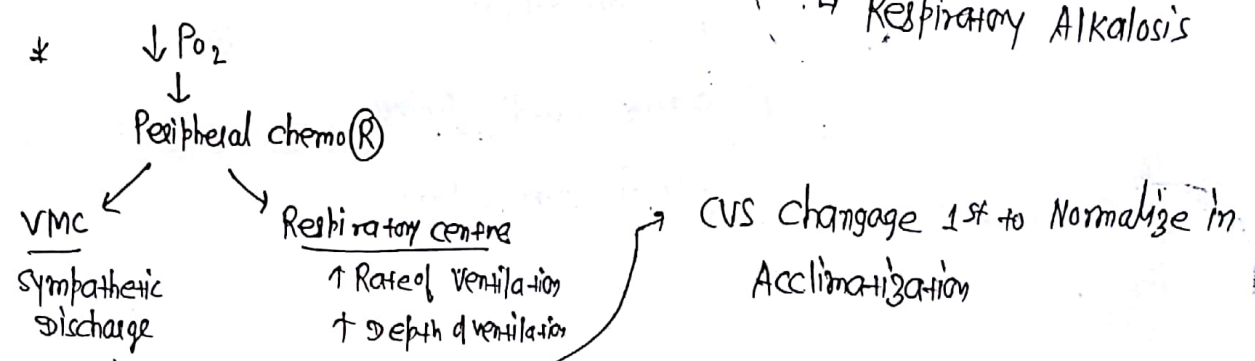
- Development of compensatory Mechanism to ward off ill effects of low Barometric pressure
- i) \uparrow Renal excretion of bicarbonates
 \downarrow PH tends to Normalize (so, Respiratory Alkalosis; further not \downarrow P_{O_2} \rightarrow less Respiratory drive
 \rightarrow comes from kidney \rightarrow \uparrow Red cell mass (Polycythemia)
Leads to Polyuria (More loss of water) Inhibit the peripheral chemo- (O₂ Receptor)
- ii) \downarrow P_{O_2} \rightarrow \uparrow Erythropoietin \rightarrow \uparrow Red cell mass (Polycythemia)
- iii) Shifts oxygen-Hb dissociation curves to Right (Least helpful) \Rightarrow at less O_2 delivery to tissue
- * In Natives of High Altitude \Rightarrow iv) \uparrow capillary density at tissue level
v) \uparrow Mitochondria; \uparrow cytochrome enzyme

HIGH ALTITUDE PHYSIOLOGY

($\downarrow P_{O_2}$) Hypoxic Hypoxia \rightarrow Stimulate Peripheral chemo Receptor \rightarrow \uparrow Rate of ventric
 \uparrow Depth of ventila

$P_{O_2} \propto \frac{1}{V_A}$

 "CO₂ washout" \Leftarrow Hyperventilation
 \rightarrow Respiratory Alkalosis



* Physical activity during Acclimatization \rightarrow Rate of Ascend
Individual Susceptibility alter 1st 24 hrs. (1-3 days)
 \Rightarrow on low \bar{c} in few hours

ACUTE MOUNTAIN SICKNESS

Mild Altitude Sickness \Rightarrow

Headache; sleep disturbance; Irritability.

HACE \Rightarrow High altitude cerebral edema

$\downarrow P_{O_2}$

\downarrow
Cerebral vasodilation

\downarrow

$\uparrow P_c$

\downarrow
 \uparrow Tissue Fluid formation

$R_x \Rightarrow$ give O_2 & evacuate

Prevention \Rightarrow Acetazolamide

\hookrightarrow Produces Metabolic acidosis & Acidosis res. Respiratory drive

HAPE \Rightarrow High altitude Pulmonary edema

$\downarrow P_{O_2}$

\downarrow

Not Uniform vasoconstriction \leftarrow Pulmonary Vasoconstriction (Patchy vasoconstriction)

\uparrow Flow in those Areas

Where there is little or No Vasoconstriction.

\downarrow

$\uparrow P_c$

\downarrow
 \uparrow Tissue Fluid formation

CHRONIC MOUNTAIN SICKNESS

\hookrightarrow MONGE'S DISEASE

\hookrightarrow occur in Fully Acclimatized patient

$\downarrow P_{O_2}$

\downarrow

Pulm. Vasoconstriction

\downarrow

Pulm. Hypertension

$\downarrow P_{O_2}$

\downarrow

\uparrow Red cell Mass

\downarrow

\uparrow Blood Viscosity

\downarrow

\uparrow Resistance to flow

Right heart Failure

\downarrow

Congestive Cardiac Failure

\hookrightarrow Pulmonary edema

GI T

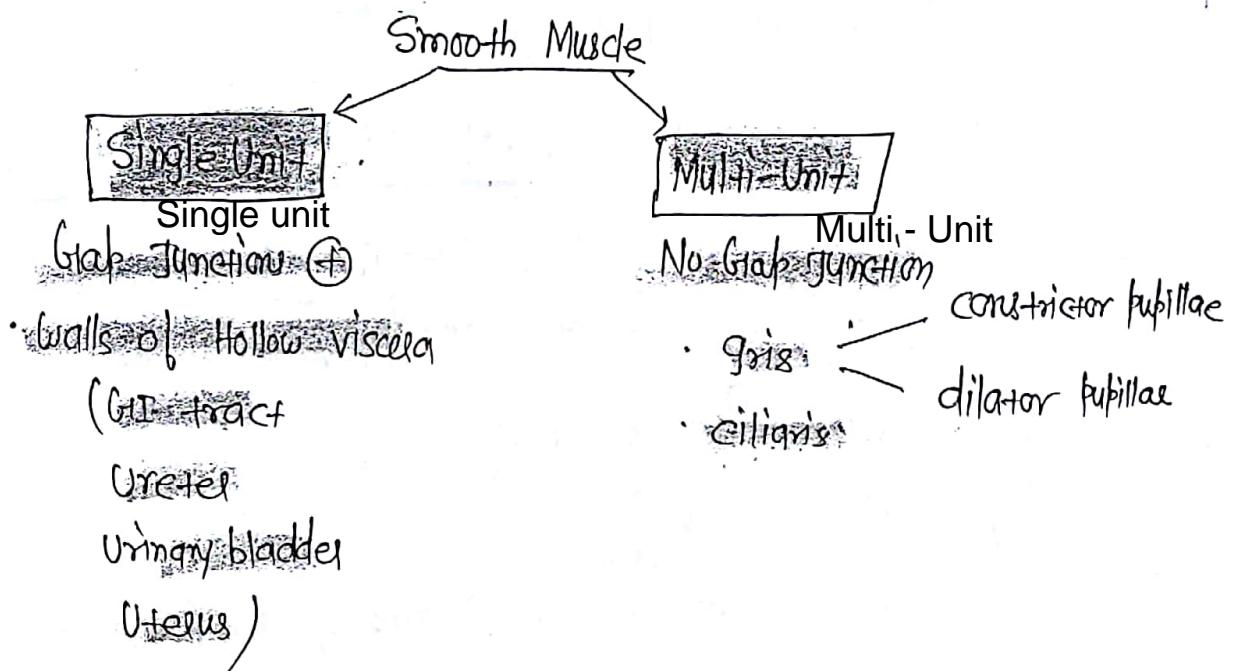
Smooth Muscle

- Unstriated
- Involuntary
- Actin
- Myosin
- Tropomyosin
- Troponin
- ~~Ca²⁺ Binding Protein~~ Ca⁺⁺ binding protein

Gate keeper in the GI T
↓
Epithelial calcium channel

RMP of Smooth Muscle
↓
-60 mv to -30mv

→ Calmodulin
Calmodulin



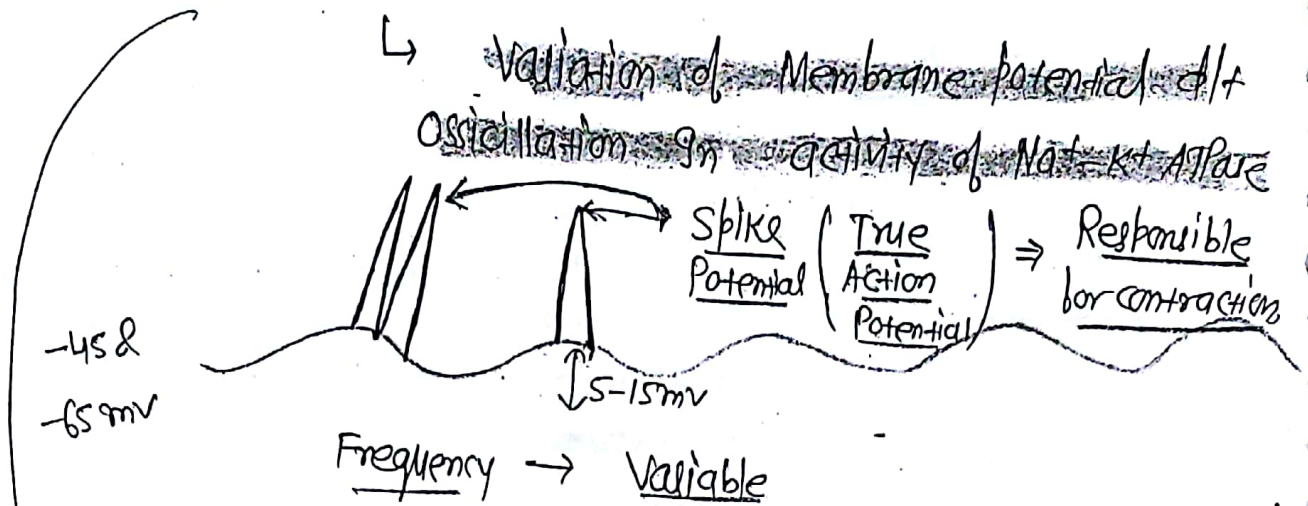
* Vascular Smooth Muscle ⇒ has both single & multi-unit type of Smooth Muscle

* Electrical activity
↓

Pacemaker ⇒ Interstitial cells of CAJAL

↓
BER (Basal electrical Rhythm)

* Basal electrical Rhythm



Maxim	→	Duodenum	12/min
Minim	→	Cecum	2/min

It is Not Responsible for contraction.

Depolarization ⇒ Ca^{+2} Influx (Not Na^+ Influx)

Q. ↑ frequency of spike potential in all except ⇒
↳ ↑ contractile Activity

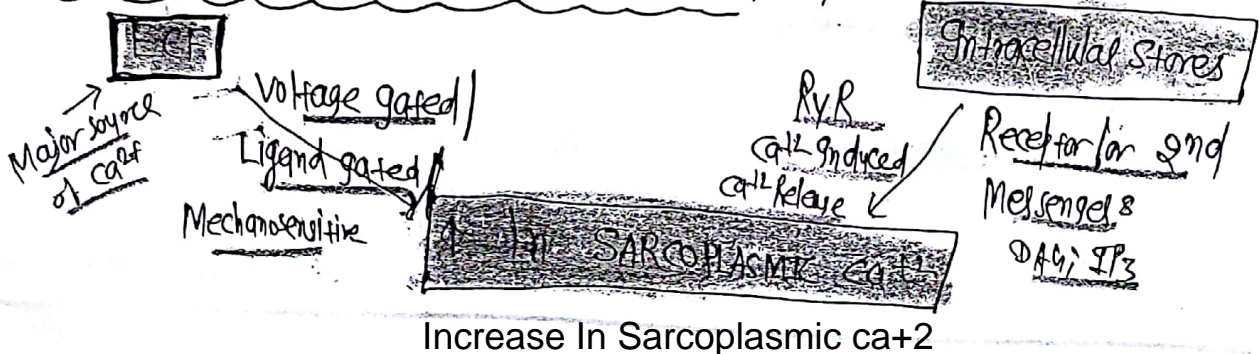
(a) Parasympathetic

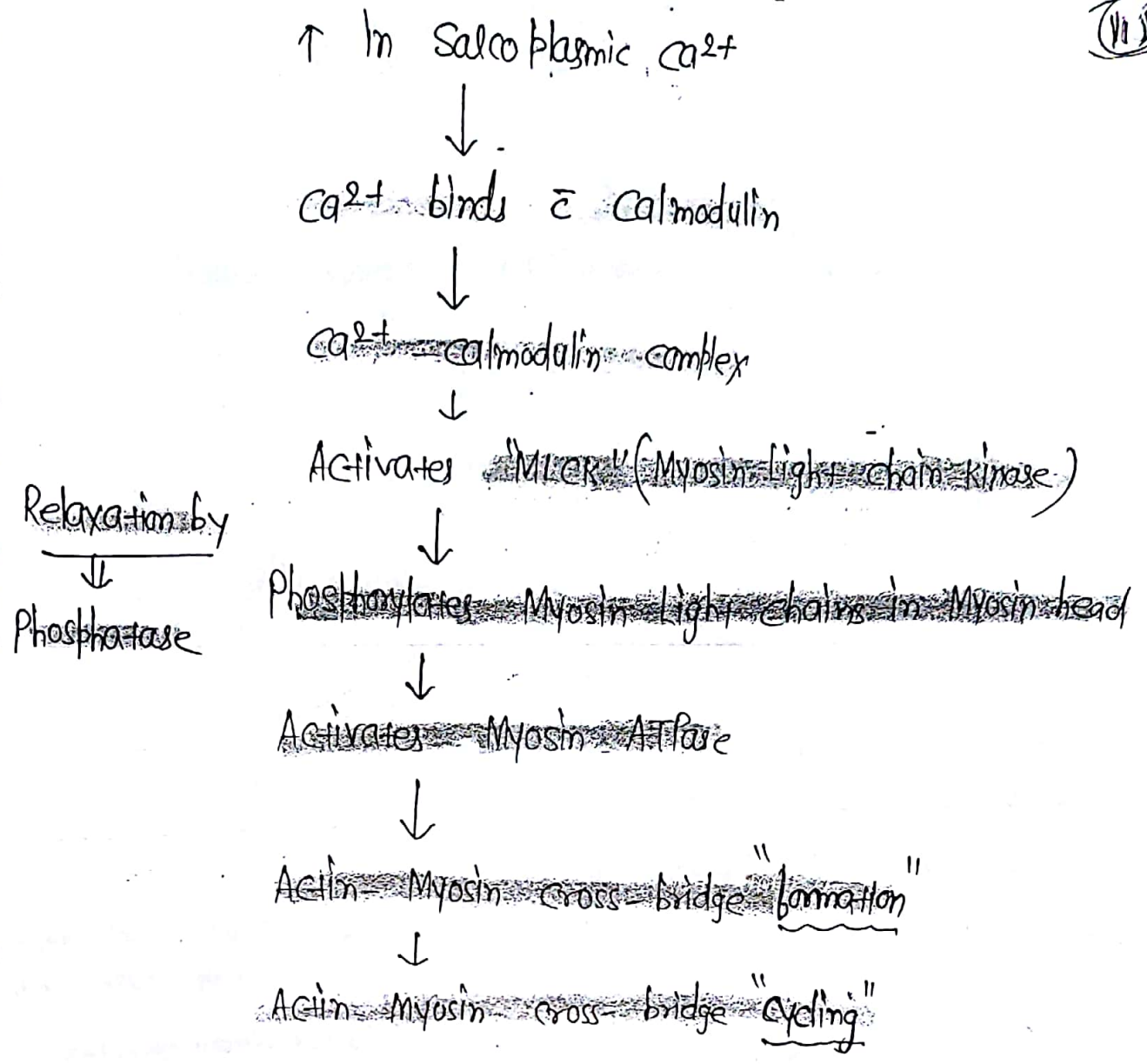
(b) Ach

(c) Stretch → Opening of Mechano-sensitive Ca^{+2} channel.

~~(d) Adrenaline~~

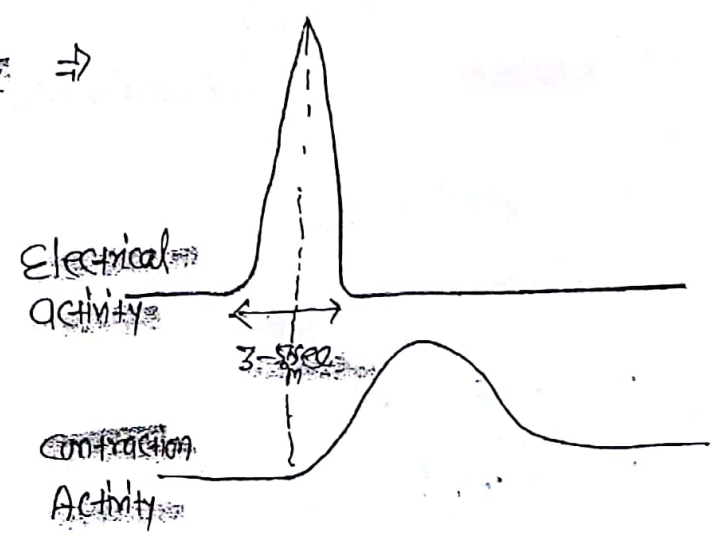
Mechanism of Smooth Muscle contraction ⇒





LATCH MECHANISM ⇒ Slower Actin-Myosin cross bridge cycling.

In Skeletal Muscle ⇒



* In Smooth Muscle

Electrical
Activity

50ms

Contractile
Activity

150ms

* GI Transplant done Rarely; b/c Intestine is Rich in Lymphoid tissue; so, chance of Graft Rejection is very high.

CONTROL OF SMOOTH MUSCLE (GI Tract)

NEURAL CONTROL

Neural control

HORMONAL CONTROL

Hormonal control

Enteric Nervous
System

Enteric Nervous
system

Intrinsic nervous system

Extrinsic nervous system

INTRINSIC
NERVOUS SYSTEM

EXTRINSIC
NERVOUS SYSTEM

Found in
blw the
longitudinal
& circular
muscle
layers

MYENTERIC
OR
AUBERBACH'S
PLEXUS

SUB MUCOSAL
OR
MEISSNER'S PLEXUS

↓ controls

Controls Gut
Motility

- Secretory Activities
- Blood supply

Contraction of sphincters
↓ the contractile activity
↓ secretory activities

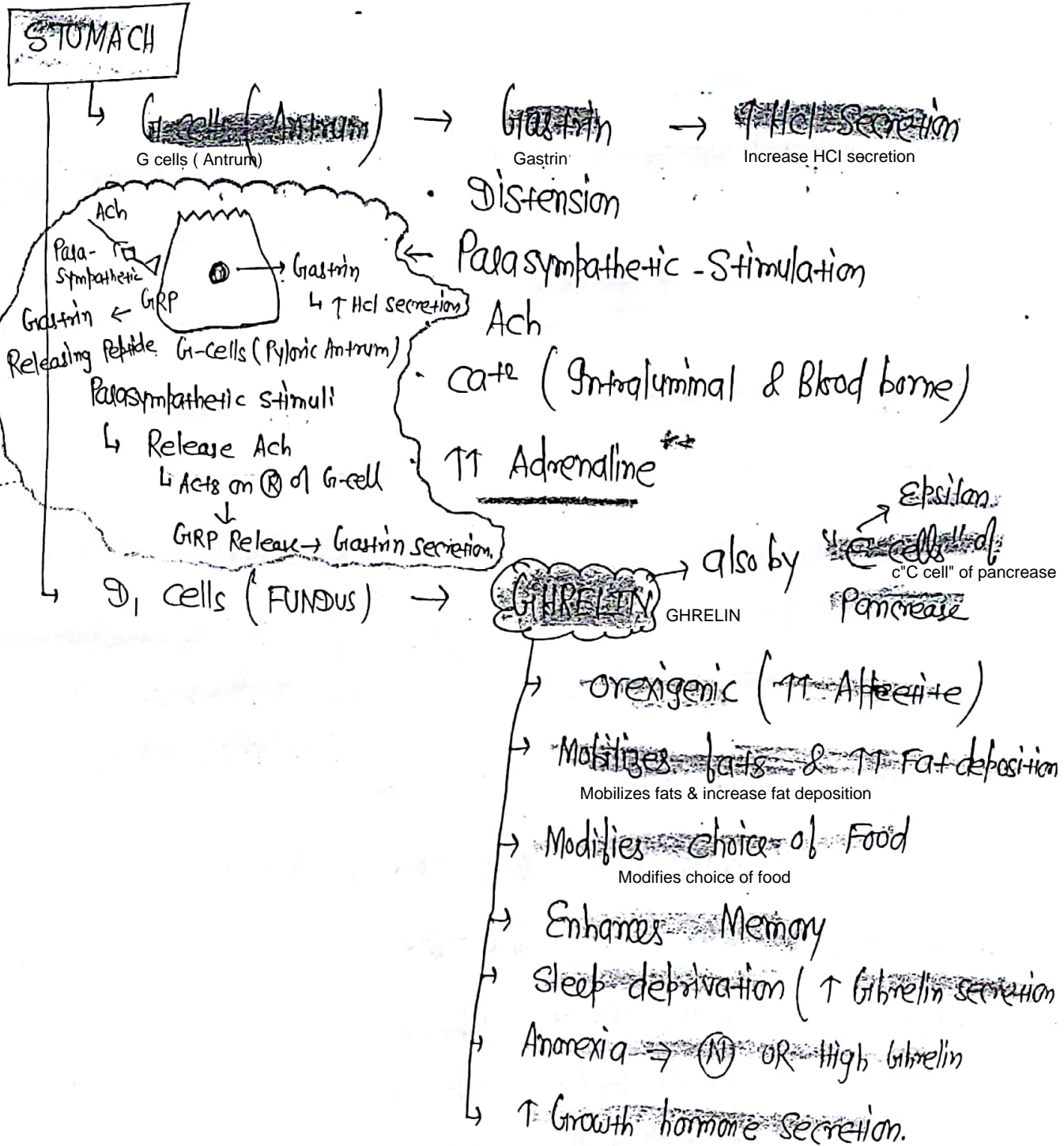
↑ Sympathetic

Parasympathetic (↑ contractile activity
of gut)

- Relaxation of sphincters
- ↑ secretory activities

HORMONAL CONTROL OF GI Tract

116



Small intestine
SMALL INTESTINE

↳ I cells ⇒ CCK

- ↑ Gall bladder contraction
- ↑ Pancreatic enzyme secretion
- Potentiates action of secretin

Q9 Most imp. Stimulation for secretion of CCK is
 (A) Fatty acids; (B) Products of Protein Digestion

CHOLERETICS Choleretics

• ~~↑ synthesis of bile salts~~

Increase synthesis of bile salts



• ~~↑ secretion of bile~~

Increase secretion of Bile

eg ⇒ ~~bile salts~~

Bile salts

CHOLEGOGUES Cholegogues

• ~~↑ Gall bladder contraction~~

Increase Gall Bladder contraction



• ~~↑ secretion of bile~~

Increase secretion of Bile

~~CCK~~

CCK

"S" cells of Small Intestine ⇒ SECRETIN

"S" cells of small intestine

↳ ~~↑ HCO₃⁻ content of~~
 Increase HCO₃⁻ content of

bile & pancreatic juice

bile & pancreatic juice

~~delays gastric emptying~~

delays gastric emptying

Q9 Most alkaline secretion is

Saliva → 6.0 - 8.0 (7-8 usually)

Bile → 7.0 - 8.0

Pancreatic juice → up to 8.8

Brunner's gland → up to 9.3

Secretion ↳ ⊕ in duodenum

"K" cells of Small Intestine ⇒

k cells of small intestine

GIP ⇒ Glucose dependent Insulinotropic peptide
 Glucose dependent Insulinotropic peptide

Incretin

Incretin

↑ Insulin

Increase Insulin

"L" cells of Small Intestine ⇒

"L" cells of small intestine

GLP-1

GLP-1

Glucagon like peptide

Glucagon like peptide

~~GIP-1~~ ⇒ ↑ Insulin

GIP - 1

⇒ klas "Physiologic β -cell stimulating hormone of GI tract"

"Physiology Beta-cell stimulating hormone of GI tract"

117

δ cells of Small Intestine

Somatostatin

Somatostatin

↓ Gastric Motility & secretion
Decrease - Motility & Secretion

↓ Intestinal "

Decrease Intestinal motility & secretion

M cells of Small Intestine

Motilin

Erythromycin combines c Motilin

→ When a Meal is ingested, secretion of Motilin is suppressed until digestion & Absorption are complete

↳ Migratory Motor Complexes

↑ Gut Motility (QQ)

HORMONES OF GI Tract

Hormones of GI Tract

Gastrin family

Gastrin
CCK

Structural Similarity

Secretin family

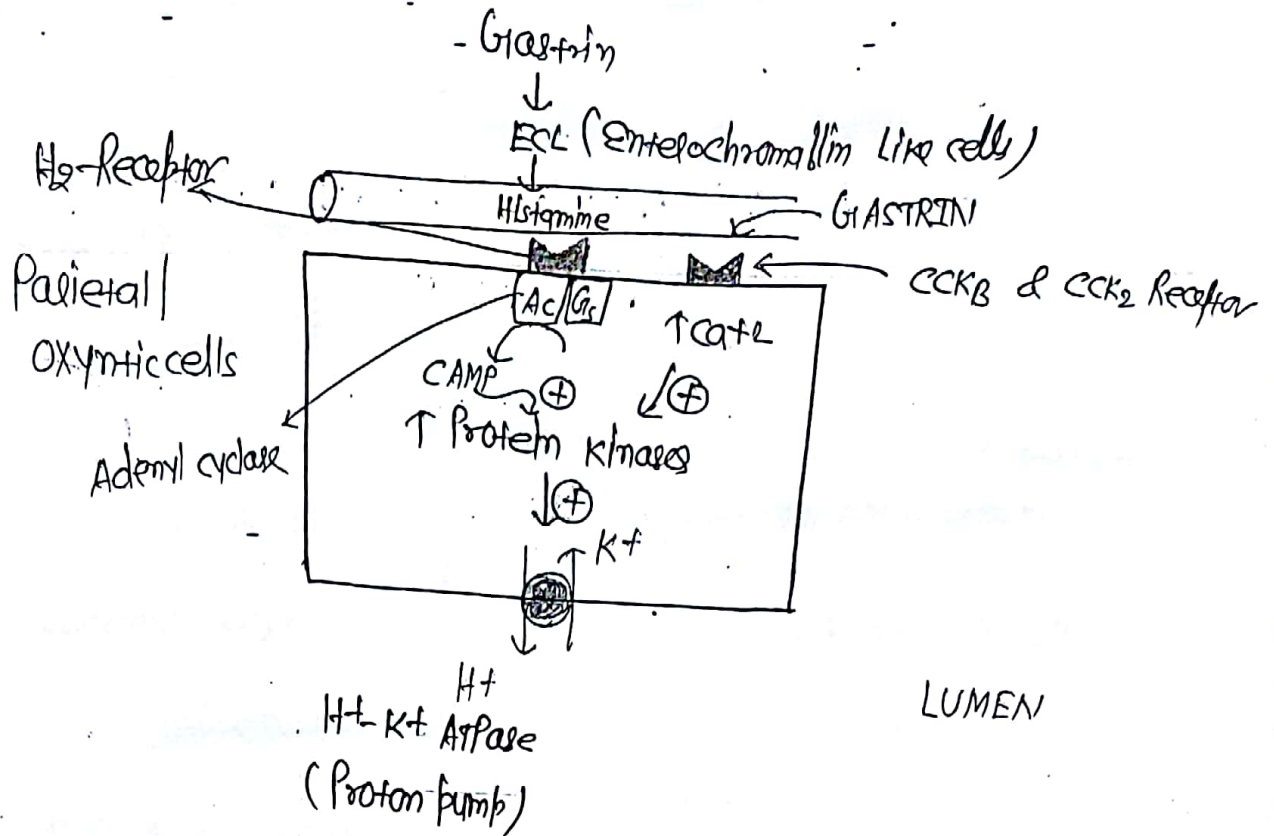
Secretin

GIP

GIP-1

Somatostatin

Motilin



* Gastrin acts on entero-chromaffin cells
 ↓
 Histamine secretion
 ↓
 Acts on H₂ Receptor
 ↓
 acts on G_s Protein
 ↓
 Activates Adenyl cyclase
 ↓
 ↑ cAMP & ↑ Protein kinases
 Increase cAMP & Increase Protein kinase

SECRETION OF GI TRACT

SALIVA

⇒

800-1200 ml/day

pH = 6.0-8.0 (usually 7.0-8.0)

- 3 Pairs of Major salivary gland

→ Parotid → Largest gland

→ Submandibular → Max^m contribution to

→ Sublingual Saliva

3 Phases

(118)

↳ **CEPHALIC** ⇒ Most Important ; b/c Thought, sight
ORAL → by Sour Maxim, Smell
GASTRIC activated

3 Enzymes

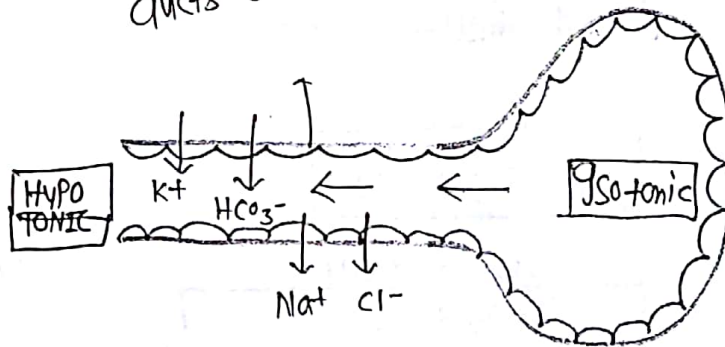
↳ S. Amylase

Lysozyme

Lingual Lipase ⇒ Secreted by 'EBNER'S' GLANDS ON
DORSUM OF GLAND.

↳ Chloride ion (Cl^-) Require to activation of S. Amylase
Not H^+ , HCO_3^-

ducts are impermeable to water



Na^+ , Cl^- Reabsorption > K^+ , HCO_3^- Secretion into saliva

* Aldosterone Receptors are pres. here

↳ In collecting duct

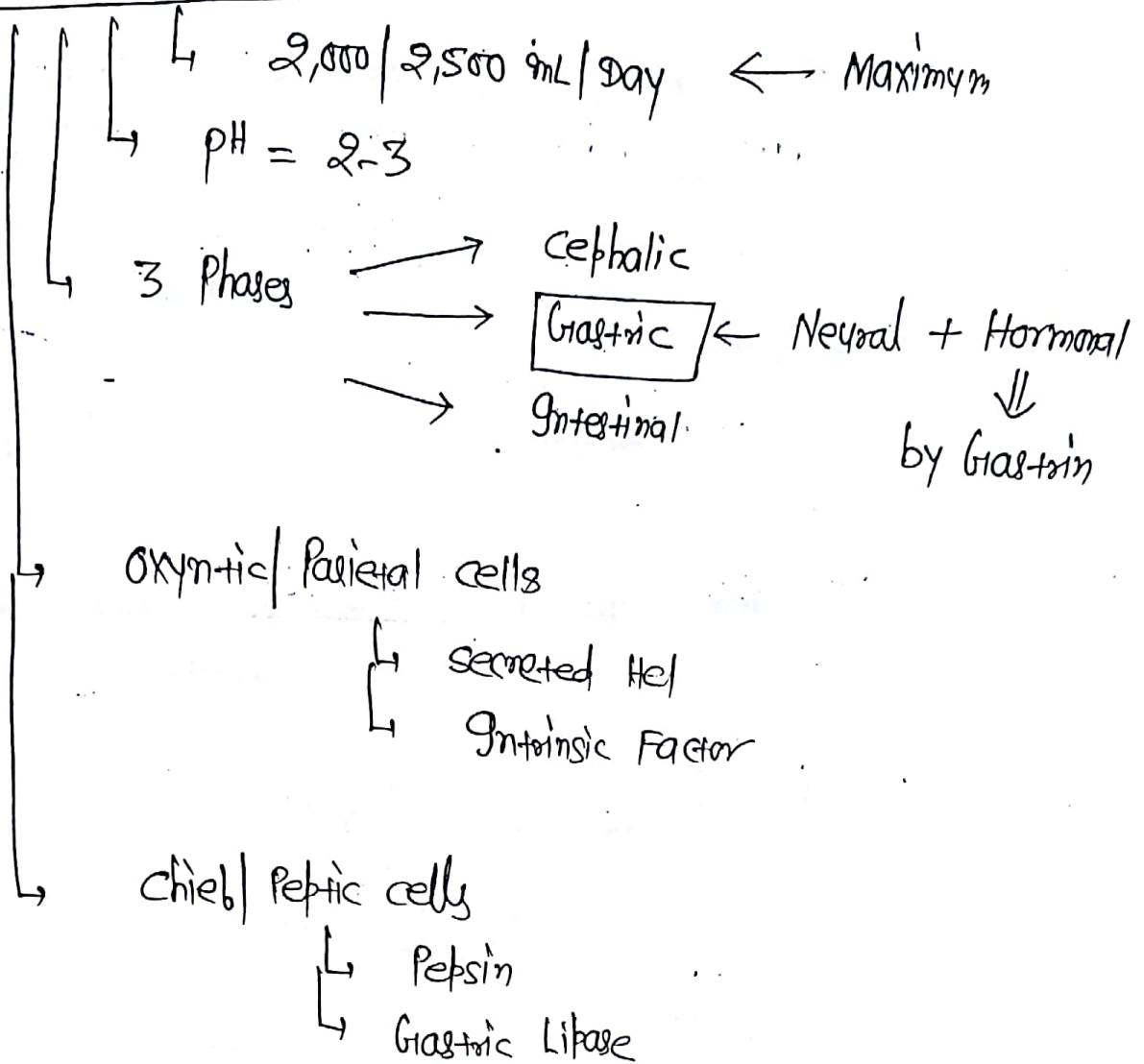
Salivary glands

Sweat glands

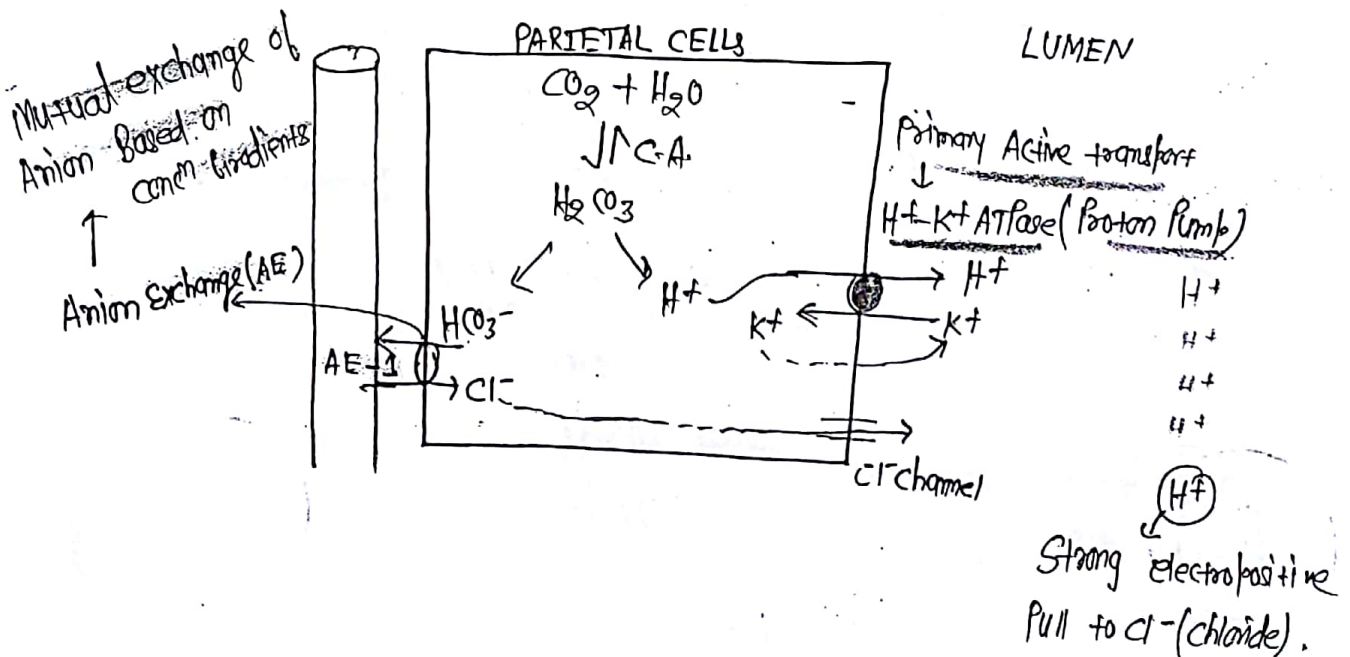
Colon

Hippocampus

GASTRIC SECRETION \Rightarrow



HCl Secretion

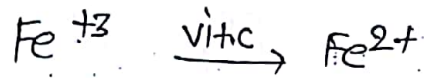


Function of HCl \Rightarrow i) Bactericidal Agent

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pH of Pure HCl \Rightarrow 1-2.

ii) Solubilizes the Iron salts



\hookrightarrow only absorbable form of Iron

iii) - Activation of Pepsinogen to form Pepsin.

PANCREATIC SECRETION

\Rightarrow 1500 mL/day

\hookrightarrow pH = up to 8-8

\hookrightarrow very Rich in enzyme

\hookrightarrow Pancreatic Amylase

• Trypsin

• Chymotrypsin

• Carboxypeptidase

• Elastase

• Nucleotidase

• Lipases

\hookrightarrow Colipase dependent Pancreatic Lipases

\hookrightarrow Bile Salt activated Pancreatic Lipases

INTESTINAL SECRETION \Rightarrow 1500 mL/day

\hookrightarrow pH = 7.0-8.0

\hookrightarrow Secrete Enzymes

\Downarrow
EnteroKinases

Trypsinogen $\xrightarrow{\quad\quad\quad}$ Trypsin

\Downarrow
Activates all other Pancreatic enzyme to their active form.

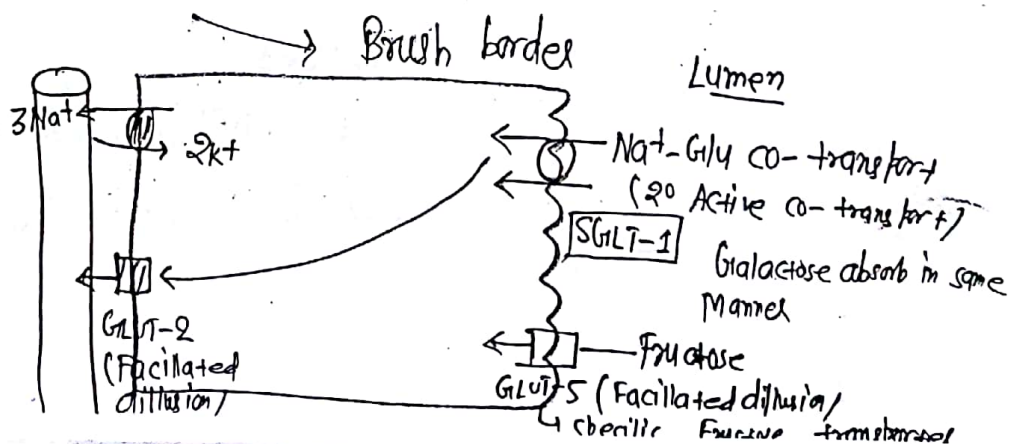
• Disaccharidases

$\left\{ \begin{array}{l} \rightarrow \text{Lactases} \\ \rightarrow \text{Succrases} \\ \rightarrow \text{Maltases} \end{array} \right.$

• Di & Tri-peptidases

DIGESTION & ABSORPTION

① CARBOHYDRATE $\xrightarrow{\quad\quad\quad}$ Luminal



Glucose is absorbed by :-

a) ~~Facillated diffusion~~

b) ~~2°~~ Active co-transport

120

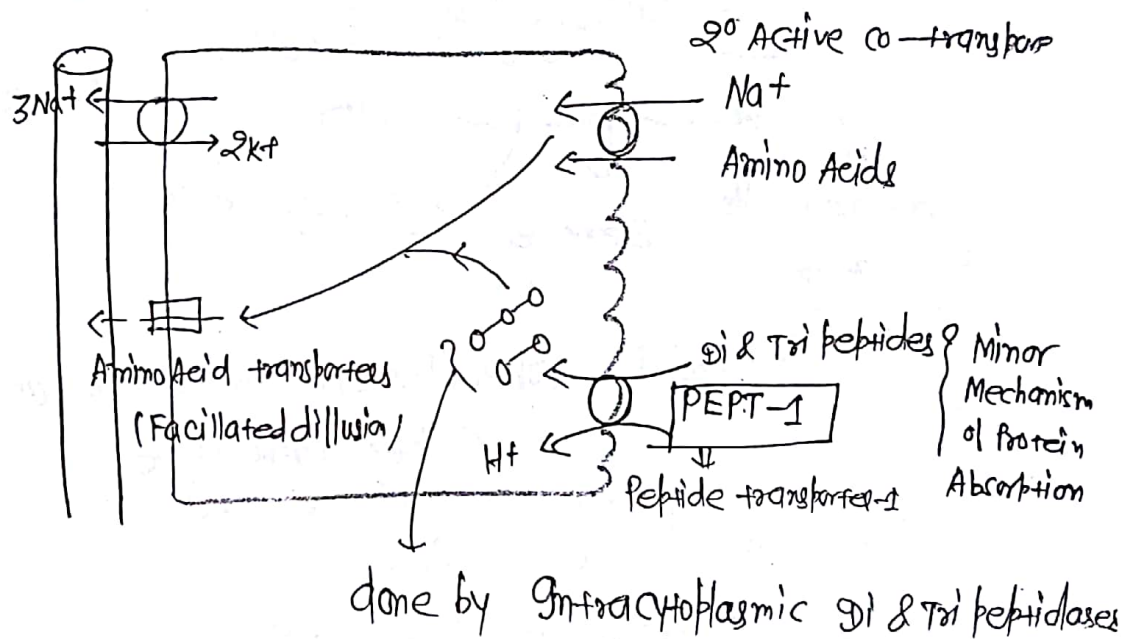
(B) PROTEINS DIGESTION :-

Luminal digestion

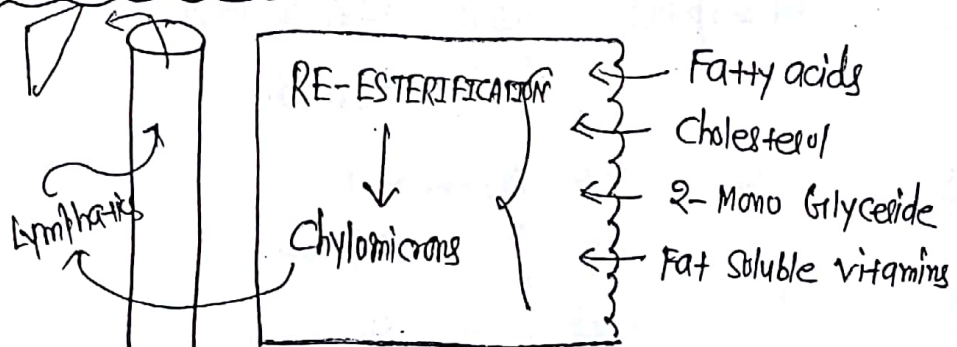
Brush border digestion

Intracytoplasmic Digestion (Di & Tri peptidase)
(+)

Absorption \Rightarrow

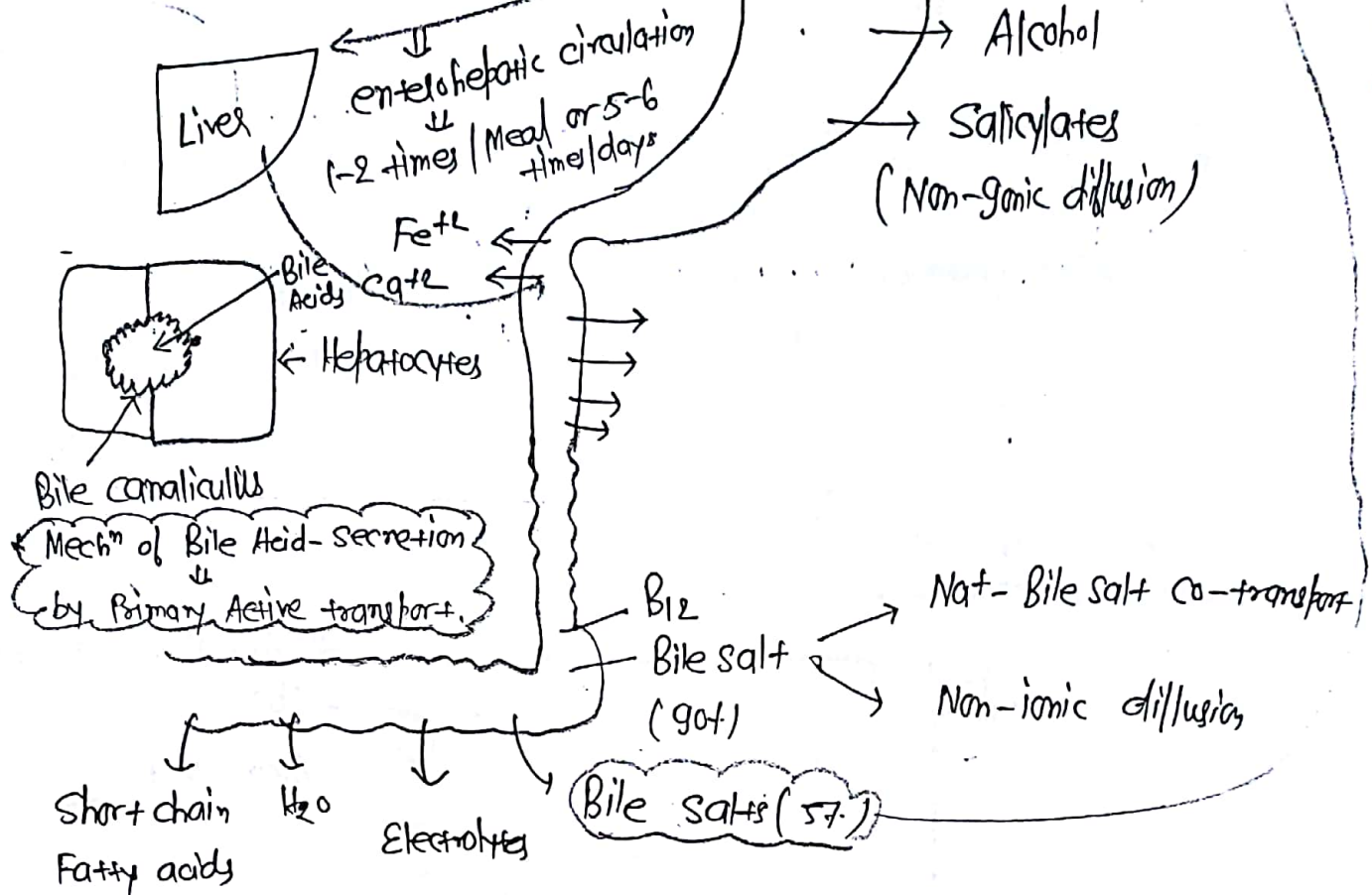


(C) FATS ABSORPTION :-



* ABSORPTION →

Stomach ⇒ organ for storage
but absorb alcohol; Salicylates



↳ Produced by colonic bacteria by Action on dietary fibres;
complex carbohydrate

eg ⇒ Acetate 60%
Propionate 25%
Butyrate 15%

Q. Absorption alcohol starts in 11
↳ Stomach

Q. Max^m Alcohol Absorption 12
↳ Jejunum

Q. Fe²⁺ absorption ⇒ Duodenum

Q. Max^m Ca²⁺ \Rightarrow Jejunum

(12)

Q. B₁₂ \Rightarrow Distal ileum

Q. Fatty acids \Rightarrow Jejunum

Q. Bile ~~Acids~~ ^{Salts} \Rightarrow Distal ileum

Q. Short chain fatty acids \Rightarrow colon

Q. Long chain fatty acids \Rightarrow Jejunum

Q. Max^m water absorption \Rightarrow 9000 ml enters in ~~sf.~~ ^{Small intestine}

Jejunum \rightarrow 5500 mL (Max^m)

Ileum \rightarrow 200 mL

Colon \rightarrow 1300 mL

Feces \rightarrow 200 mL

Q. Max^m Na⁺ absorption \Rightarrow Jejunum

Q. Max^m K⁺ is secreted by \Rightarrow Salivary glands

- Q. Max^m K⁺ concⁿ is in \Rightarrow Colonic fluid

SDA (Specific Dynamic Action of Food) \Rightarrow

\hookrightarrow Obligatory Expenditure of Energy for Digestion & Absorption of Food

eg \Rightarrow	<u>Proteins</u>	<u>Carbohydrate</u>	<u>Fats</u>
	$\downarrow \otimes$ amount	$\downarrow \otimes$ amount	$\downarrow \otimes$ amount
	100 Kcal energy generated	100 Kcal energy generated	100 Kcal energy generated
To digest & assimilate \Rightarrow	30 Kcal expend	6 Kcal	5 Kcal

Q. Q. SDA is Max^m for \Rightarrow Proteins

BASAL METABOLIC RATE

depends \Rightarrow ~~Body Surface Area~~
on ~~Lean Body Mass~~

MOVEMENTS OF GIT Tract

Movements of GI Tract

* When food prt. in Small Intestine

\hookrightarrow first Movement \Rightarrow i) Segmentation Contraction \Rightarrow

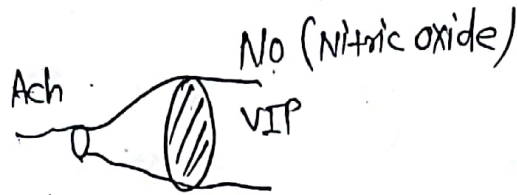
• Mixing contraction

• Alternate contraction & Relaxation in the segment of Intestine

ii) Peristalsis → Local Neural activities

(22)

↳ Mediated by Parasympathetic & Sympathetic



Ring of
contraction
behind food

Relaxation
in front of food

In Esophageal Peristalsis

1°
↓
Mediated by
vagus during
swallowing

2°
↓
ib Primary fails to
move food forward
↓
Secondary (2°) is mediated
by local plexus

In B/L vagotomy

↳ Loss of 1° Esophageal
Peristalsis

iii) Migratory Motor Complexes (MMC)

Migratory motor complexes (MMC)

⊕ In Inter Digestive Period

Not a Neural activity, it is Hormonal activity

↓
by Motilin (M cells)

↳ Ring of contraction which starts from body of
Stomach → goes upto distal ileum

↳ K/as "HOUSEKEEPING CONTRACTION"

Housekeeping contraction

1st MMC \Rightarrow 90-120 min after Last Meal

\downarrow then

occur in cycles of 90 min

- Phases of MMC \rightarrow
- I \Rightarrow Quiescent Phase
 - II \Rightarrow Phase of irregular electrical & Motor activity
 - III \Rightarrow Phase of Regular electrical & Motor activity

Total duration \Rightarrow 90 min

MMC \Rightarrow 5 cm/min

(Peristalsis \Rightarrow 5-25 cm/sec)

It prevents Reflux of Colonic contents into ileum, and also clearing the tract.

GI REFLEXES

* Receptive Relaxation of Stomach

Receptive relaxation of stomach

- Relaxation of Fundus during Swallowing
- Mediated by vagus



* Gastro colic Reflex \Rightarrow

(123)

Food \oplus in Stomach \Rightarrow Defecation
In Infants it is pr., Abolished in Adults.

Q. Max^m Postprandial \uparrow in tone & Motility is \oplus in
Which Segment of colon?

- a) Ascending colon
- ~~b) Descending colon~~
- ~~c) Sigmoid colon~~

* ENTEROGASTRIC REFLEX \Rightarrow Neural + Hormonal
 \hookrightarrow Mainly Somatostatin



\downarrow Gastric Motility
 \downarrow Gastric secretion

Stimuli that inhibit \Rightarrow ① Distension M.gnt
Gastric Motility

② Type of Food \oplus

Fats > Proteins > Carbohydrate

③ Acidity of Gastric chyme

More Acidity of Gastric Chyme

\hookrightarrow Greater Inhibition

④ Osmolality of Gastric chyme

DEFECATION REFLEX \Rightarrow 1st Urge \Rightarrow 18 mm of Hg

Evacuation \Rightarrow 55 mm of Hg

MICTURATION REFLEX \Rightarrow 1st Urge \Rightarrow 150 ml

Uncontrollable \Rightarrow 400 ml

DEEP SEA PHYSIOLOGY

Deep Sea Physiology

① At 100 ft \Rightarrow 4 atm Pressure

At 100 m \Rightarrow 11 atm

Diver

100% $O_2 \rightarrow$ $\uparrow\uparrow$ Solubility of O_2

\downarrow

Generation of Free Radicals (H_2O_2 , O_3^-)

\downarrow

O_2 TOXICIFY - Symptom \Rightarrow Choking

~~coughing~~ coughing

So, O_2 is inert gas given

$\hookrightarrow O_2 - N_2$

Under water \Rightarrow $\uparrow\uparrow\uparrow$ Solubility of $N_2 \Rightarrow$ \uparrow N_2 Dissolution in Plasma, Myelin, Cell Membrane

\downarrow

Klas "RAPTURES OF DEPTHS"

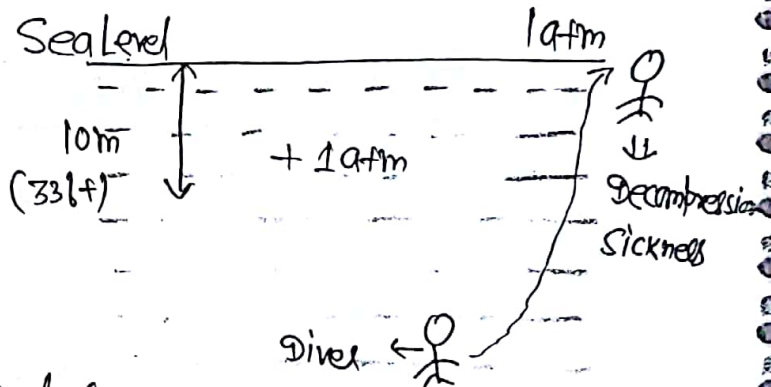
OR

"MARTINI Effect"

N_2 Narcosis

\Leftarrow Alters Ionic Conductivity

\hookrightarrow Symptoms \Rightarrow Similar to Alcohol Intoxication



TO Avoid N_2 Narcosis \Rightarrow Oxygen-He Mixture preferred

(129)

\downarrow
b/c He is less soluble

less Narcotic

less dense \Rightarrow Breathing is easier

Decompression Sickness

DECOMPRESSION SICKNESS \Rightarrow K/a "Dysbarism"

Dysbarism

OR

"CAISSON'S DISEASE"

Caisson's disease

\swarrow Gas Embolism (+)
 \swarrow M/c Symptoms \Rightarrow BENDS (Painful joint & Muscle)

Pulmonary symptoms

Cerebral symptoms

Coma
death

(+)ve "g" Forces

\uparrow Peripheral pooling of blood



"Black out"

Prevention \Rightarrow "Anti-g" Suits

(-)ve "g" forces

\downarrow \uparrow Flow towards head ends

"Red out"

\Rightarrow \uparrow Conjunctival & scleral congestion

ENDOCRINE SYSTEM

(126)

LIPID SOLUBLE HORMONES

⇒

WATER SOLUBLE HORMONES

- Steroids
- Thyroid

- Amines
- Peptides

* Synthesize as & when needed
(No storage).

↳ except ⇒ Thyroid

• Transported as Proteins

except ⇒ DHEA

Adrenal Androgen

• Transported as Such

except ⇒ GHF-1

↳ a/w growth hormone
Longer half life than
Growth hormone

• Cytoplasmic / Nuclear Receptors

• Membrane Surface Receptor

• Need 2nd Messengers

(except ⇒ Insulin)

↳ b/c Insulin Receptor
itself has Tyrosine kinase activity.

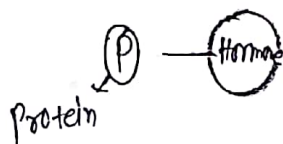
• Mechⁿ of Action ⇒ Synthesis of
New proteins (enzyme)

• Act by Modifying Action
of Pre-existing enzyme

• Longer half Life

• Shorter half Life

Total Hormone = Bound hormone + Free hormone



Activity (Responsible for Activity
as well as for feedback)

* Liver Induces \Rightarrow \uparrow Hepatic output of Proteins

- Estrogen
- Barbiturates
- opioids
- Major Tranquilizers

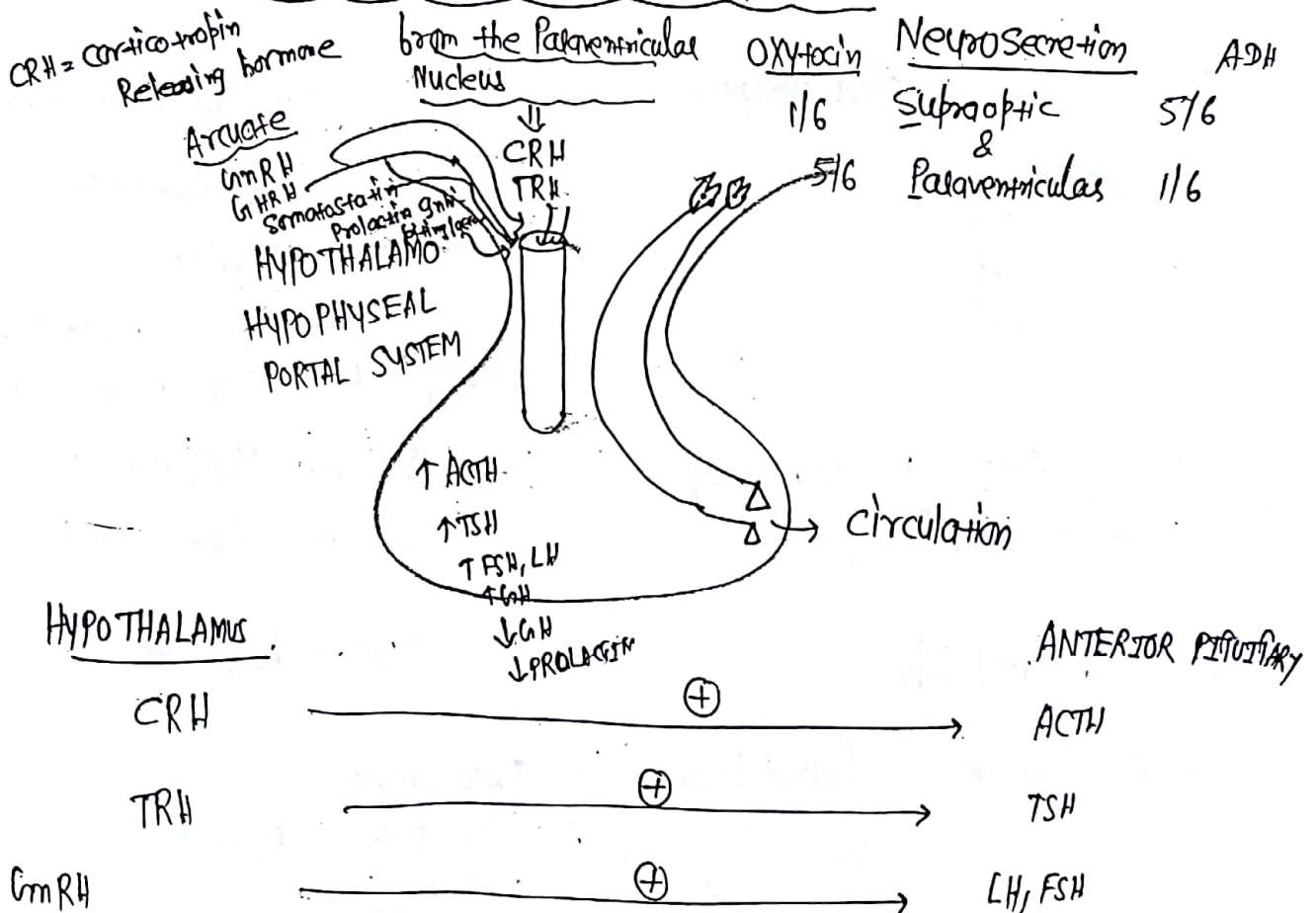
\downarrow
 \uparrow Bound hormones ; & \downarrow free hormone
 (Transient) change

\downarrow
 \uparrow total hormones ; \uparrow Bound hormone ;
 Free hormones (N)

Q In a heroin Addict

\hookrightarrow Total thyroid \Rightarrow Tes
 Bound thyroid \Rightarrow Tes
 Free $T_3, T_4 \Rightarrow$ (N)

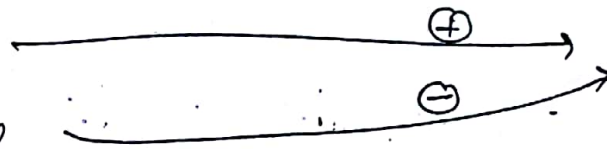
HYPOTHALAMIC PITUITARY AXIS



HYPOTHALAMUS

GHRH

Somatostatin



ANT. PITUITARY ²⁵⁷ (27)
GH

Prolactin inhibiting factor (Dopamine) \rightarrow Prolactin

"STALK Effect" \Rightarrow \uparrow in Prolactin

\hookrightarrow Thrombus in Hypothalamo Hypophyseal Portal system

* All Hypothalamic hormone are secreted in Pulsatile fashion \Rightarrow except \Rightarrow TRH

* Low frequency Pulse of GnRH $\longrightarrow \uparrow$ FSH

High frequency Pulse of GnRH $\longrightarrow \uparrow$ LH

Q. Q. continuous Infusion of GnRH

$\hookrightarrow \downarrow$ FSH; \downarrow LH (down Regulation of GnRH happen in continuous Infusion)

* Pulsatile secretion prevents down Regulation of GnRH Receptor in Anterior Pituitary

ANTERIOR PITUITARY

Acidophils \Rightarrow

Max^m in No.

Somatotrophs \Rightarrow GH

\swarrow Lactotrophs \Rightarrow Prolactin

Basophils \Rightarrow

Corticotrophs \Rightarrow ACTH

Gonadotrophs \Rightarrow FSH, LH

Thyrotrophs \Rightarrow TSH

\swarrow Min^m in No.

GROWTH HORMONE

Stimuli which tes GH \Rightarrow

Stress Hormone

\uparrow Energy Substrates

eg \Rightarrow • Catecholamines

• Growth hormones

• Glucocorticoids

• Glucagon

• ADH

• Thyroid \pm

• Fasting;

• Starvation;

• Hypoglycemia; - Most potent stimulation

• Stress hormone

• Emotion

• Sleep (NREM III, IV)

[In REM sleep \Rightarrow \downarrow Growth hormone]

• Arginine; Leucine

• Exercise

• Ghrelin

ACTIONS OF GROWTH HORMONE

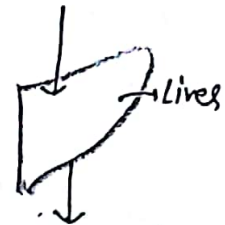
128

DIRECT ACTIONS

- ↑ Blood glucose level
(Anti-insulin action)
- ↑ Free Fatty acids
(Lipolysis)
- ↑ Protein synthesis
- Na^+ , K^+ , Ca^{2+} , Phosphorus Retention

INDIRECT ACTIONS

GH



IGF-1 (Source → Liver)
(Somatomedin-C)

- ↓ Blood glucose
- Lipogenesis
- Protein synthesis
- Chondrogenesis
(Growth of epiphyseal plate control)

Responsible for
"Growth Spurt @ Puberty"

IGF-1 Secretion is Max^m in ⇒ Adolescence > Children > Adults > Elderly

Growth hormone

IGF-1 Synergistic IGF-1

Action on Growth hormone

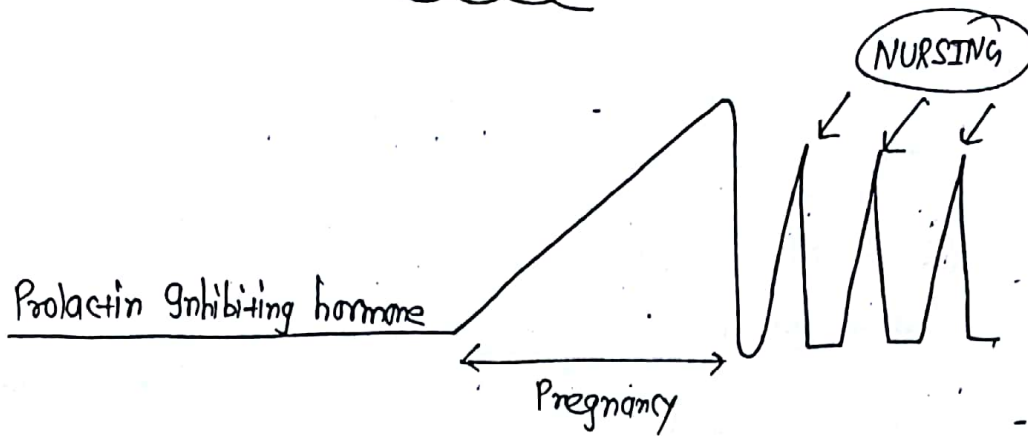
↑ IGF-1
Receptor on
Cartilage

Direct Action (Independent Action)

CARTILAGE

⇒ Estrogen causes fusion of growth plate
* only IGF-1 in short stature child

PROLACTIN



Stimuli for Prolactin →

New PET SHOP

New ⇒ Nursing

P ⇒ Pregnancy

E ⇒ Estrogen

T ⇒ TRH (Hypo-thyroidism → Galactorrhea)

S ⇒ Stress
Strenuous exercise
Sleep (NREM)

S ⇒ Sexual intercourse

H ⇒ Hypo-thyroidism

O ⇒ Opiates

P ⇒ phenothiazines

Stimulation Test ⇒ TRH Stimulation test ⇒ TSH, PRL

GnRH " ⇒ FSH, LH

Insulin Infusion test ⇒ GH, ACTH

POSTERIOR PITUTARY

129

ADH

* Stimuli which Tes ADH \Rightarrow ① \uparrow Plasma Osmolality;
(Tes of 5 mosm) \uparrow Most potent stimulus

② \downarrow Blood volume (10-15%)

③ Stress;

④ Emotions;

⑤ Pain;

⑥ Trauma;

⑦ Surgery;

⑧ Nausea;

⑨ Vomiting;

⑩ Exercise;

⑪ Prolonged standing;

⑫ clonidine; carbamazepine

⑬ Angiotensin II

* Stimuli which \downarrow es ADH \Rightarrow ① \downarrow Plasma Osmolality

② \uparrow Blood volume

③ Alcohol

④ Weightlessness

* Receptors for ADH \Rightarrow

V_1/V_{1A}
Receptors

V_2 Receptors

V_3/V_{1B} Receptors

V_1/V_{1A}
 V_2
 V_3/V_{1B}

Secondary Messengers

IP_3 & Ca^{2+}

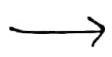
\Rightarrow Vascular Smooth Muscle \rightarrow Vasospasm
 \Rightarrow Liver \rightarrow Glycogenolysis
 \Rightarrow Area Prostate \rightarrow \downarrow Cardiac output
 \Rightarrow Collecting duct \Rightarrow \uparrow Insertion of $A\beta-2$ on Luminal Membrane

IP_3 & Ca^{2+}

\Rightarrow Ant. Pituitary \Rightarrow \uparrow ACTH secretion

THYROID HORMONES

Hypothalamus



TRH

\ominus

\oplus

TSH

\ominus

T_4, T_3

Steps in Synthesis of Thyroid hormone \Rightarrow ① IODIDE TRAPPING \Rightarrow
 In Thyroid cells

In Colloid \Rightarrow

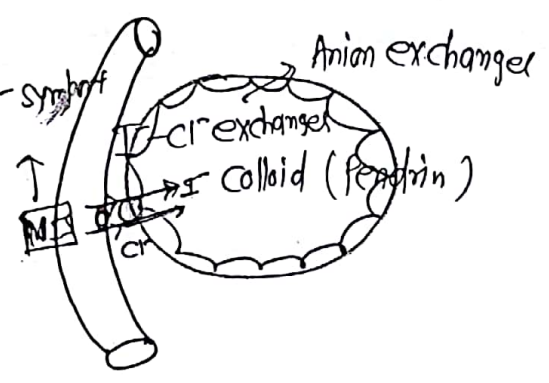
\rightarrow Oxidation of $I^- \xrightarrow{TPO} I_2$

\rightarrow Iodination of Tyrosine

$\begin{cases} MIT \\ DIT \end{cases}$

Enzyme
 Thyroid Peroxidase (TPO)

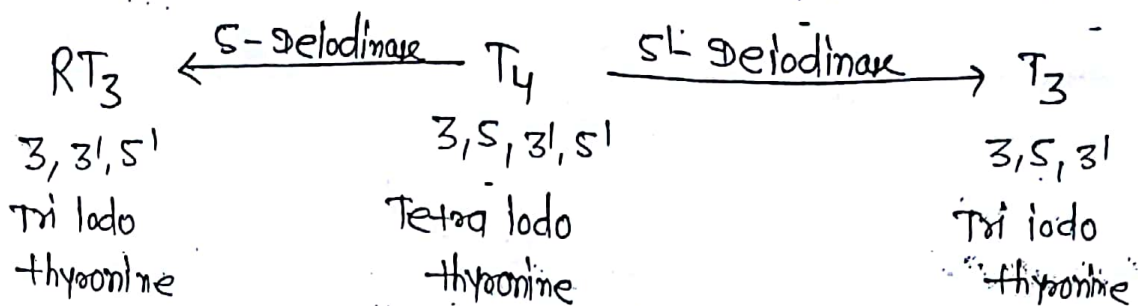
\uparrow Na⁺-I⁻ symport
 \uparrow 2^o Active Co-transport



\rightarrow Coupling Rx^n

$MIT + MIT \rightarrow T_4$ TPO

$MIT + DIT \rightarrow T_3$ TPO



→ Reverse T₃
Q. RT₃ In circulation. — Main Source

(A) Secretion

~~(B) Peripheral conversion of T₄ → RT₃~~

Condⁿ In which RT₃ > T₃ (Advantage)

- Starvation → Conserves calories
- Prolonged illness
- Chronic kidney disease
- Febate illness
- Burns
- "Se" deficiency
- Drugs which inhibit deiodinase

* Action of Thyroid hormone : ⇒

① ↑ ~~O₂ consumption~~ (↑ BMR, ↑ Body temp, ↓ body weight)
 Increase O₂ consumption (Increase BMR, Increase Body Temp., Loss of body weight)

⇒

except
 except

Pituitary;

Spleen;

Lymph Node;

Ovaries;

Testis.

(2)

~~Hypothyroid~~
Hypothyroid~~Carotenemia~~
Carotenemia +

(31)

b/c;

~~Carotene~~
Carotene~~Thyroid~~
Thyroid~~Vitamin A~~
Vitamin A

(3)

~~Hypothyroid~~
Hypothyroid~~1. Serum cholesterol~~
Increase serum cholesterol.

b/c;

~~Thyroid~~
Thyroid~~2. Normal LDL Receptor~~
Increase of LDL receptor~~4. So, serum cholesterol~~
So, decrease serum cholesterol

(4)

Protein Metabolism

Protein Anabolic effect; but in larger dose Protein catabolic effect.

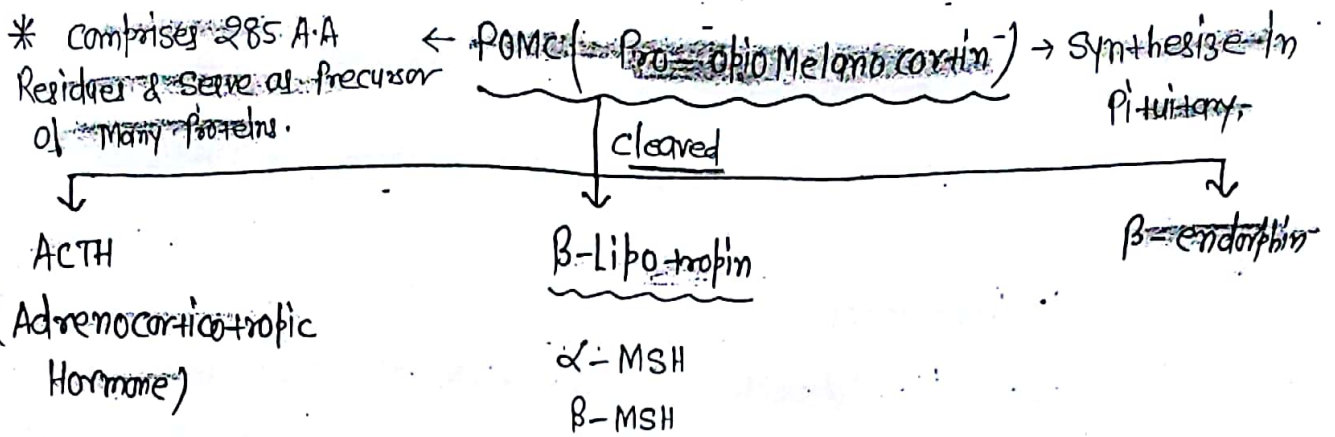
* ~~TR α~~ , ~~TR β~~ , ~~TR γ~~ , Receptors are widely distributed; TR β is found only in the brain.ADRENALS *** Layer of Adrenal cortex \Rightarrow ~~Zona glomerulosa~~Hormone secretion **
~~Aldosterone~~ (Mineralocorticoids)~~Zona Fasciculata~~

Glucocorticoids (cortisol; cortisosterone); & some amounts of Androgen

~~Zona Reticularis~~

Sex Steroids (Androgens); & some amounts of Glucocorticoids

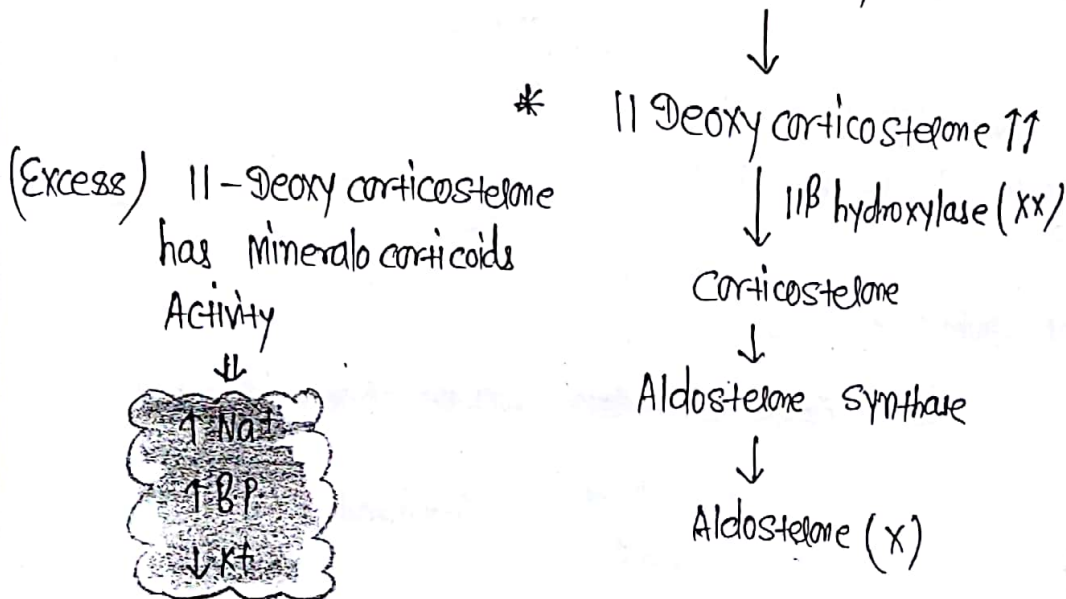
* Hormone secreted by Adrenal Medulla \Rightarrow Epinephrine
(epinephrine > Nor epinephrine)
(90%) Nor epinephrine* After Hypophysectomy \hookrightarrow ~~Zona glomerulosa~~ will be intact (RAAS); while~~Zona Fasciculata~~ } \rightarrow Atrophied.
~~Zona Reticularis~~



• Cushings ⇒ Hyperpigmentation

↳ ↑↑ ACTH (S. ACTH itself has Melanocyte Stimulating hormonal activity).

* Deficiency	Aldosterone	Glucocorticoids	Androgens
• 21 β hydroxylase (95% of CAH) No Mineralocorticoid Activity	↓	↓	↑↑ (Virilizing symptom)
• 11 β hydroxylase (5% of CAH) Mineralocorticoid Activity	↓	↓	↑↑
How to differentiate ⇒	↑ B.P. ↓ K ⁺ } Seen in 11β hydroxylase deficiency ⇒ HypoAldosteremic Hypertension		



* Deficiency	Aldosterone	Glucocorticoids	Androgens ⁽³²⁾
17,20 Lyase deficiency	↑	↓	↓

~~** 17,α hydroxylase deficiency~~

* GLUCO-CORTICOIDS ACTION ⇒

Glucocorticoids ↓ ⇒

B ⇒ Basophils	} By promoting their migration from blood into tissues
E ⇒ Eosinophils	
L ⇒ Lymphocytes	

Glucocorticoids ↑ ⇒

- Neutrophils
- Monocyte
- RBC
- Platelets

Permissive Action ⇒ It enhances the action of other hormone.

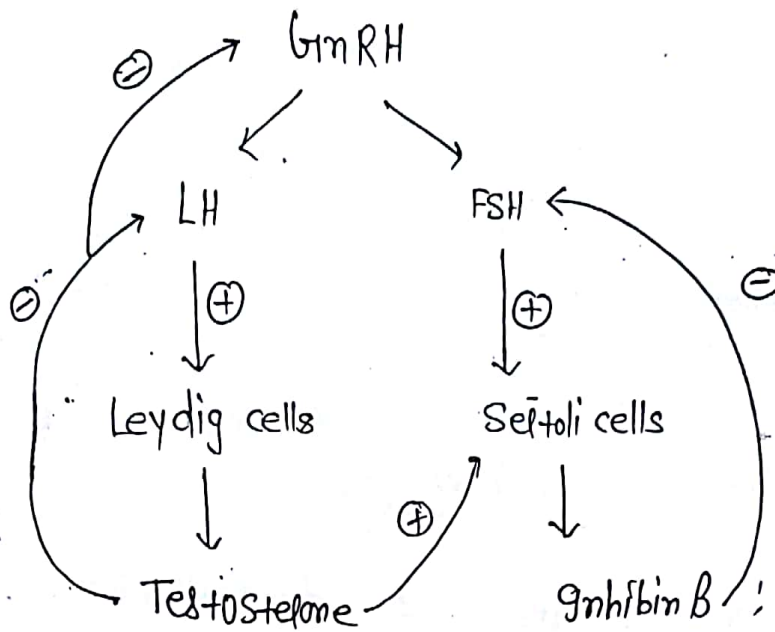
on Glucagon → • Glycogenolysis in Liver; but Not in Muscle in General; but when cortisol is ⊕ w Glucagon, do glycogenolysis in Muscle too.

• Lipolysis

on catecholamine → Glycogenolysis;
(Adrenal Medulla hormone)
Lipolysis;
Vasodilation;
Bronchodilation.

* Secretion of glucocorticoid is Regulated by ⇒ Anterior Pituitary gland through ACTH (corticotropin)

* MALE REPRODUCTIVE - HORMONE

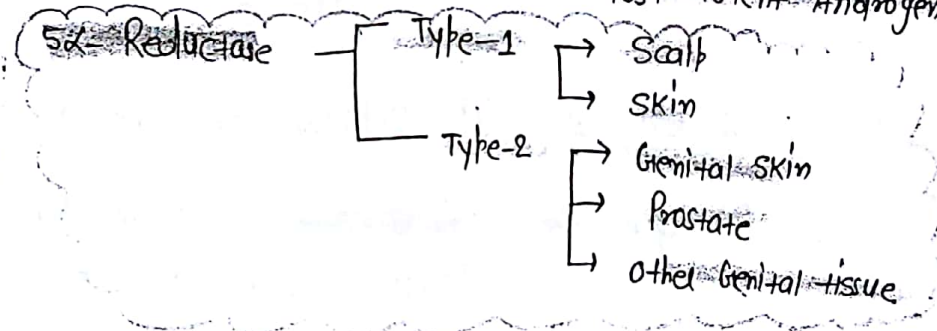


- DHT
- DHEA (dehydro-epiandrosterone)
- Androstendione

Inhibin B;
Androgen binding Protein (ABP);
Mullerian Inhibiting Substance.

* Testosterone $\xrightarrow{5\alpha\text{-Reductase}}$ Dihydrotestosterone (DHT)

Most Potent Androgen



* Action of different Androgens \Rightarrow

Fetal Life \Rightarrow Testosterone
Development of Male type
of Internal Genitalia

DHT
Male type of external
Genitalia

- Male type of brain

Testosterone

DHT

(132)

Post Puberty \Rightarrow Spermatogenesis;
Gonadotropin Regulation;
Test Muscle Mass;
Development of sexual drive

2^o sexual character
Prostate growth

Q.8.

Before Puberty castration done??

(a) Tall; (b) Dwarf; (c) Normal

\hookrightarrow d/t Lack of Estrogen (No Physcal fusion).

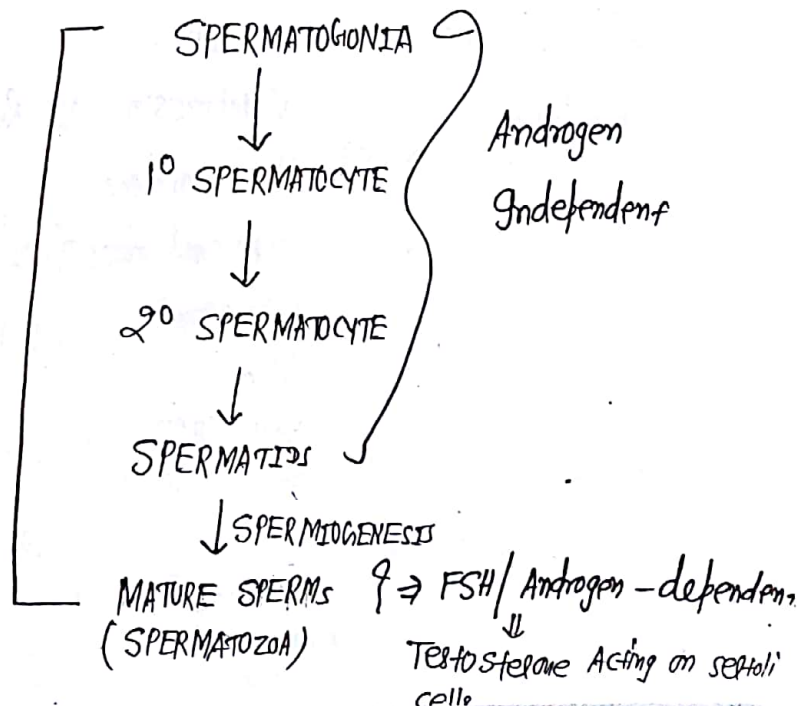
* Function of Sertoli cells \Rightarrow Supportive cells;

\hookrightarrow as blood testis barrier;
 \hookrightarrow secrete Androgen Binding Protein;
 \hookrightarrow also secrete Inhibin B; MIS (Mullerian Inhibiting substance)
 \hookrightarrow contains Aromatase

Testosterone $\xrightarrow{\text{AROMATASE}}$ Estrogen

* SPERMATOGENESIS \Rightarrow

74 days



CLASSIFICATION OF HORMONE

GROUP I :- Hormones acting on Intracellular Receptor;

GROUP II :- Hormones acting on Membrane Receptor;

IIA :- Hormones acting through cAMP;

IIB :- Hormones acting through cGMP;

IIC :- " " " IP₃ - DAG Ca²⁺ system

IID :- " " " Kinases (Tyrosine kinase; JAK-STAT kinase)

* TYPE OF RECEPTORS

1) Gi-protein coupled Receptor (GPCR) → Mechⁿ of Action →

① Via Adenylyl cyclase (AC) → Activation of Adenylyl cyclase
Results in Tes synthesis & Intracellular acylation
of cAMP.

example ⇒ CRH : → Corticotropin Releasing Hormone
LH^q, FSH^q;

TSH ;

ACTH ; (Corticotropin^q)

ADH ;

Vasopressin (V₂ Receptor)

Parathormone;

Catecholamines (β₂^q, α₂^q) eg ⇒ Adrenaline ;

Glucagon^q

hCG

Calcitonin;

Somatostatin;

Ach (M₂) ;

Dopamine^q (D₁, D₂) ;

Angiotensin II (epithelial cells) ;
L-Asn : Vasopressin (V₁)

⑥ Phospholipase IP_3 - DAG System \Rightarrow

(34)

IP_3 Mobilizes Ca^{2+} from intracellular organelles \rightarrow \uparrow cytosolic Ca^{2+}

Ca^{2+} acts as "2nd Messenger" @ here \leftarrow "DAG" enhances protein kinase

"C" activation by Ca^{2+}

* Protein kinase "C" phosphorylates various intracellular proteins (Threonine, Serine or Tyrosine Residue).

Protein kinase "C" = phosphorylates various intracellular proteins

eg \Rightarrow GHRH (Growth hormone Releasing hormone); TRH; GnRH; ADH/
Vasopressin (V_1 Receptor); Oxytocin; cholecystokinin; PDGF; Gastrin;
Catecholamines; Angiotensin II (Vascular Smooth Muscle); Substance-P;
Histamine (H_1); Muscarinic (M_1, M_3).

⑦ Channel Regulation \Rightarrow eg \Rightarrow \uparrow Ca^{2+} - β_1 -Adrenergic; \downarrow Ca^{2+} - Dopamine D_2 ; GABA_B; \uparrow K^+ - Adrenergic α_2 ; Muscarinic M_2 ; Dopamine D_2 ; GABA_B.

2. Receptors $\bar{=}$ Intrinsic ion channels - Fastest acting Receptors;
- cell surface Receptor/Ligand gated ion-channel (for Na^+ ; K^+ ; Ca^{2+} ; Cl^- ;
eg \Rightarrow Nicotinic cholinergic, GABA_A; 5HT₃ (all other 5HT Receptor are GPCR).

3. Enzyme Linked Receptor - ① Intrinsic enzyme ② Tyrosine kinase \Rightarrow Insulin; Epidermal growth factor (EGF), PDGF; FGF.

③ JAK-STAT KINASE BINDING \Rightarrow eg \Rightarrow Growth hormone; Prolactin.

④ Guanylyl cyclase \Rightarrow Result in intracellular accumulation of cGMP
eg \Rightarrow Atrial Natriuretic peptide & Nitric oxide

4. Receptors Regulating Gene expression (Transcription factors) :-
Slowest Acting.

a) Cytoplasmic Receptors → Glucocorticoids; Mineralocorticoids; Androgens; Progesterone.

b) Nuclear Receptors → Estrogen, T_3 , T_4 , Retinoic acid; vit D

SECOND MESSENGERS

- Molecules that Relay signals from the Membrane Receptors to Target Molecules inside the cell.

eg ⇒ cAMP; cGMP; Phosphatidylinositol; Diacylglycerol (DAG); IP_3 ; Ca^{2+} ; NO; CO; H_2S .

NEEDS *

So, NO acts as both 1st Messenger, through cGMP; as well as secondary messenger.

So, NO acts as both 1st messenger, through cGMP; as well as secondary messenger

* Receptor → Biological transducers

- Adequate stimulus ⇒ Stimulus to which a Receptor is Most Sensitive or to which a Receptor Respond @ Low energy Level

* Sensory coding → Receptor codes for 4 attribute of stimulus →

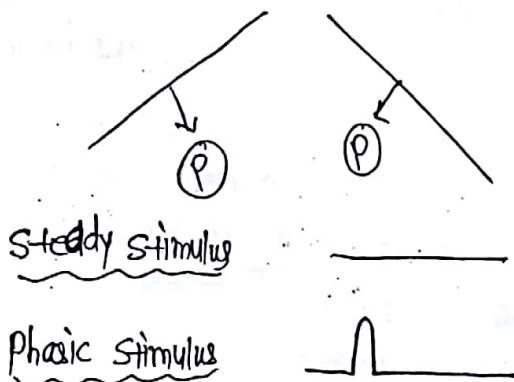
- i> Site / Location of stimulus ;
- ii> Modality (fine / crude) ;
- iii> Intensity ;
- iv> Duration .

* ADAPTATION → Stimulus ⊕ ; but Response ↓ over a Period of time

PHASIC (R)

AKA → "Rapidly Adapting (R)"

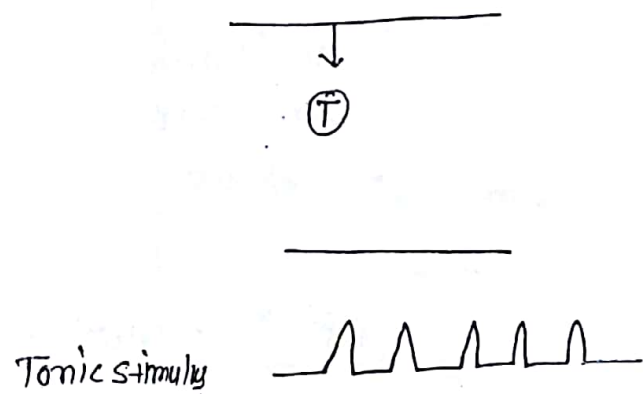
- usually encapsulated Nerve endings
- can detect Rate of change of stimulus



TONIC (R)

AKA → "Slowly Adapting (R)"

- Expanded or free (N) Nerve Ending
- can detect steady stimulus



PHASIC (R)

"AB"

eg: PACINIAN CORPUSCLES →

- Found in Joint capsules (128 Hz) & Deep in Muscles (128 Hz) & Deep in muscles

• Very Rapidly Adapting Touch

Receptor: Very rapidly adapting touch receptor

• Specific to Fast Vibration

Specific to fast vibration

(up to 800 cycles/sec) -
upto 800 cycles / sec

• Deep Pressure (Poking)

Deep pressure (Poking)

"AB"

MEISSNER'S CORPUSCLES →

Meissner's corpuscles

• Located at No hairy parts of skin
Located at No hairy parts of skin

Finger tips ++ Fingers tips ++

• Slow vibration up to 80 cycle/sec

Slow vibration upto 80 cycle/sec

• Texture (Rough/Smooth)

Texture (Rough/ smooth)

• Topognosis (Topography of Any Area; Localize by fingers)
Topognosis topography of any area: localize by fingers

• BRAILLE (writing system used by people who are blind or have low vision)

BRAILLE (writing system used by people who are blind or have low vision)

HAIR END'S ORGAN →

• Detect Light Movement on the skin
Detect light movement on the skin

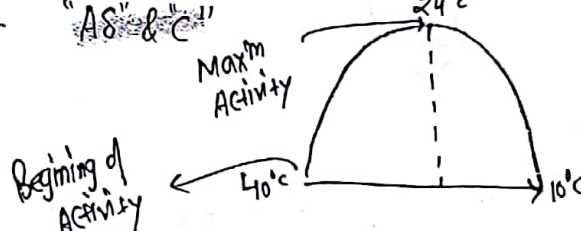
S

COLD

- More Numerous More numerous

- More cold-sensitive spots More cold-sensitive spot

- "AS" & "C"



TONIC (R)

"AB"

eg: MERKEL'S DISC →

• Fine well localized touch

• Location → At Finger tips

• Texture

• RUFFINI'S ENDING →

• Fine & well localized touch

• Prolonged Pressure

• Receptors for sense of position

C-MECHANORECEPTORS →

• Crude touch (diffuse)

• Pressure

• JOINT CAPSULE RECEPTORS →

• Muscle spindles

• Golgi tendon organs

JOINT'S POSITION SENSE

(PROPRIOCEPTION).

• BARORECEPTORS →

• Adaptation time → 2 days

• THERMORECEPTORS →

Detection of skin temperature

WARMTH

warmth

- Less in No. less is no.

- "C"

- Can detect temp. up to 30-46°C
(>46°C → Tissue damage; Pain R will stimulate)

can detect temp. upto 30-46 °c
(>46 °c => Tissue damage pain R will stimulate)

30-40 °C
 Cold receptor activity is more
 Warm - receptor activity is more
 Warm Receptor Activity is more
 Cold Receptor Activity is more
 overlap b/w cold & warmth receptors
 overlap b/w cold & warmth receptors

Other eg of Tonic (R) ⇒ NOCICEPTORS

Free Nerve endings for Pain

- Mechanical
- Thermal
- chemical
- Polymodal

very Poorly Adapting OR Not at all.

CHEMORECEPTORS

Never Adapt (b/c they give information about potentially life threatening situation)

eg ⇒ Taste buds; Osmoreceptors; olfactory (R); glucoreceptors.

QA

Don't Adapt at all

is Chemo (R); li Noci (R)

TRANSIENT RECEPTOR POTENTIAL (TRP) CHANNELS

→ These are a family of excitatory channels

Family of excitatory channels

→ Sub family

① VANILLOID (R) → Noxious Heat (Painful heat)

H+

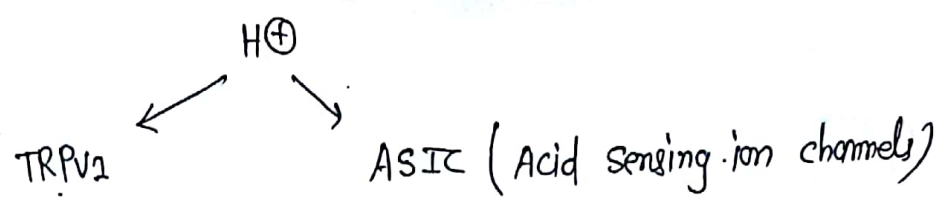
capsaicin (Vanillin group of compounds)
 Capsaicin (Vanillin group of compounds)

TRPV1 ⇒ H+ capsaicin

TRPV3 ⇒ H+ capsaicin
 detect temp b/w 35-39°C
 Detect temp b/w - 35-39°C

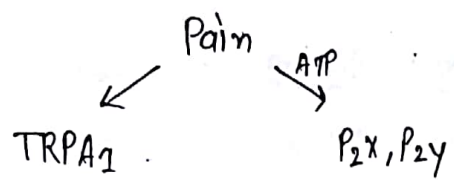
TRPV4 ⇒ detect temp up to 34°C
 Detect temp upto 34°C

② Acid sensing ion channels → detection of H^+

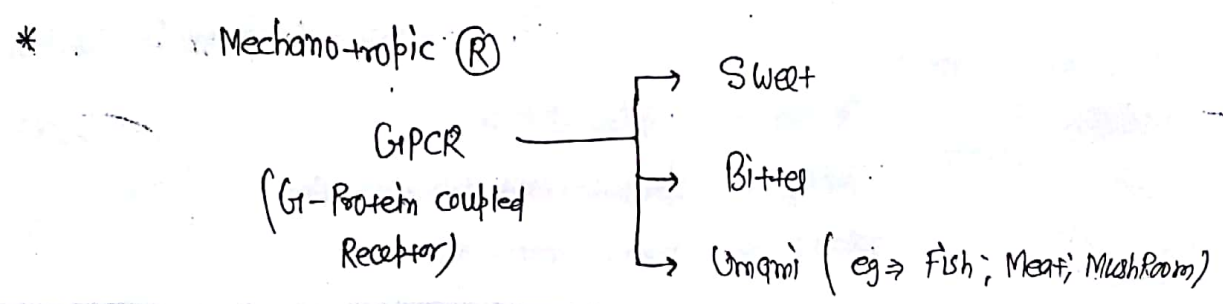
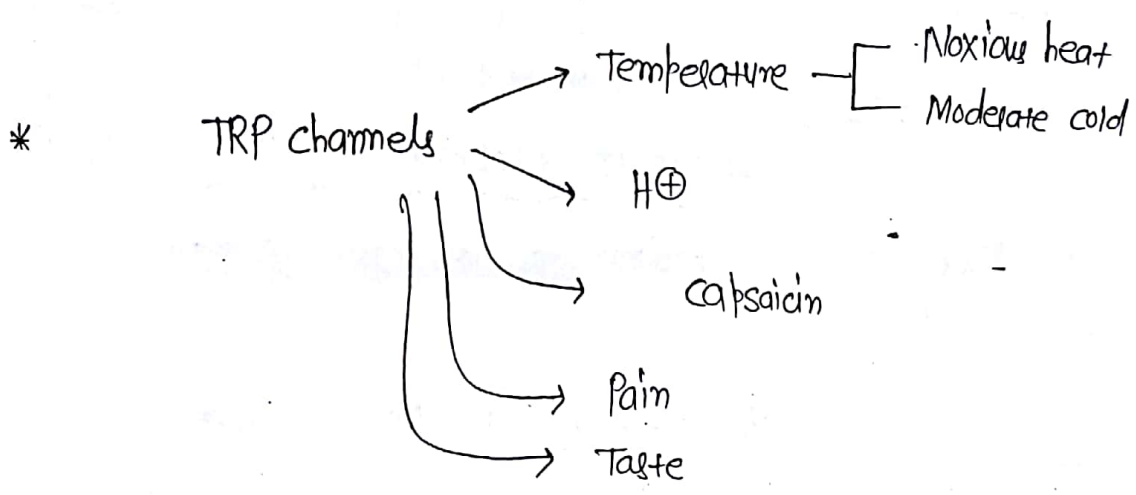


③ ANKYRIN (R) → K⁺/Ca²⁺ "TRPA₁"
Pain

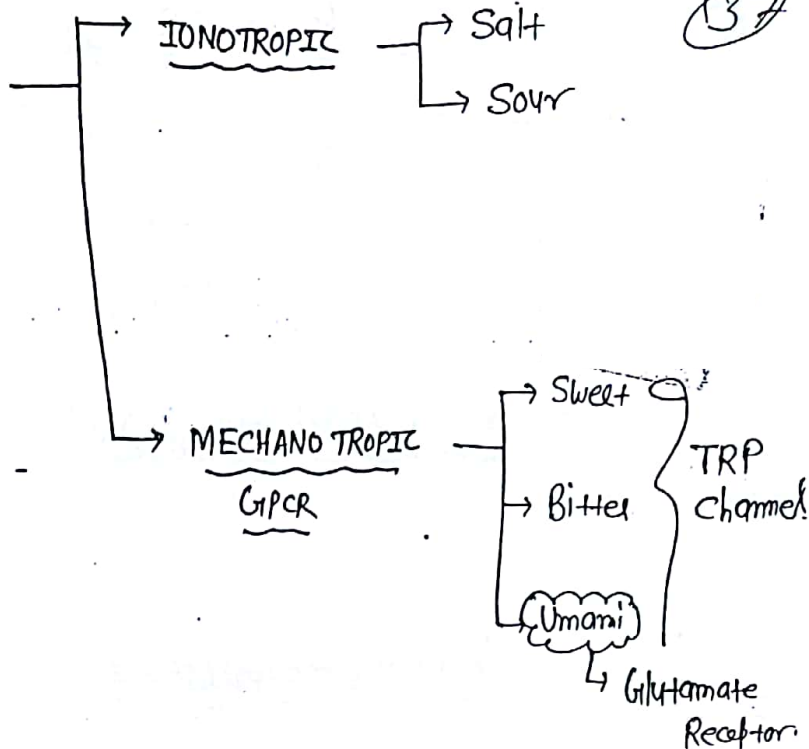
④ PURINERGIC (R) → K⁺/Ca²⁺ "P₂X, P₂Y"
Pain



⑤ MENTHOL (R) → K⁺/Ca²⁺ "TRPN₃"
 ↳ for Moderate cold
 ↳ also K⁺/Ca²⁺ "CMR-I" Receptors
 ↳ cold & Menthol sensitive Receptor-1



* Taste Receptors



NEUROTRANSMITTER

SMALL MOLECULE
RAPIDLY ACTING
NEUROTRANSMITTER

- I → Ach
- II → Amines
Nor epinephrine
epinephrine
Dopamine
Serotonin
Histamine
- III → Amino Acids
Glutamate ; Aspartate
Glycine ; GABA
- IV → Gas
Nitric oxide (NO)

LARGE MOLECULE
SLOWLY ACTING
NEUROTRANSMITTER

- Pituitary Peptides
ADH
ACTH
- Hypothalamic Peptides
GnRH
CRH
Gut Peptides
cholecystokinin (CCK)

* LAW OF SENSORY PHYSIOLOGY \Rightarrow

I. Bell-Magendie Law \Rightarrow

(Posterior) Dorsal Horn \rightarrow Sensory

(Anterior) Ventral Horn \rightarrow Motor

* DRG (Dorsal Root Ganglion) \Rightarrow contains the cell body (Soma) of sensory neuron coming from Receptor.

II. Muller's Doctrine of Specific Nerve Energy \Rightarrow

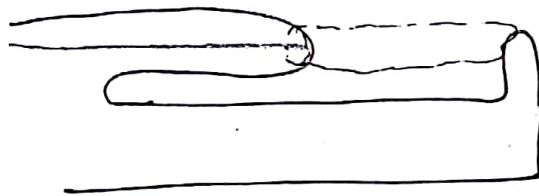
Muller's Doctrine of specific nerve energy

Receptor
Pathway
Area of Brain Stimulated

\Rightarrow Specific for Each Sensation.

III. Law of Projection \Rightarrow "PHANTOM LIMB"

- if a Nerve Pathway is stimulated Anywhere in its course; the sensation appear arising from site of Receptor.



\Rightarrow d/d cortical plasticity

Thalamus & Cortex \rightarrow Have ability to form New Synapses.

IV. Law for Intensity Discrimination of a Stimulus \Rightarrow

(A) WEBER FECHNER LAW \Rightarrow Sensation felt $\propto \log$ Intensity of stimulus

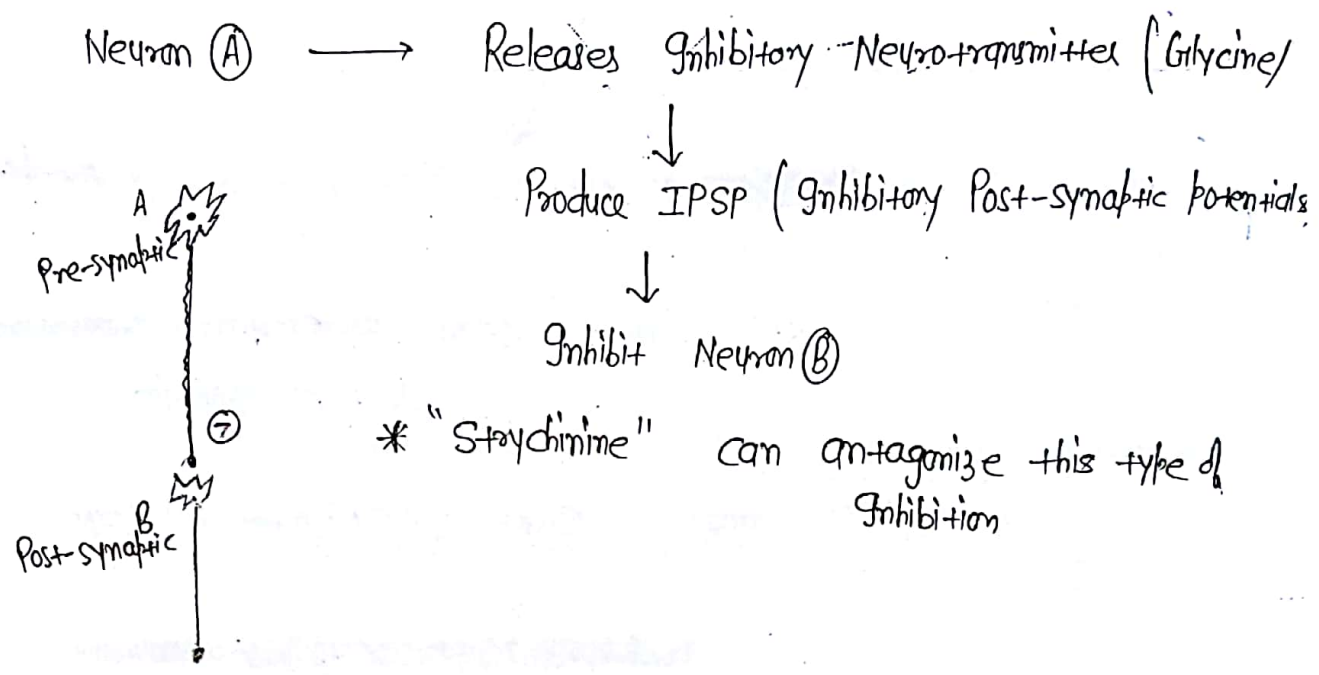
Sensation felt $2 \log$ (Intensity of stimulus)

$\Rightarrow S = K I^a$

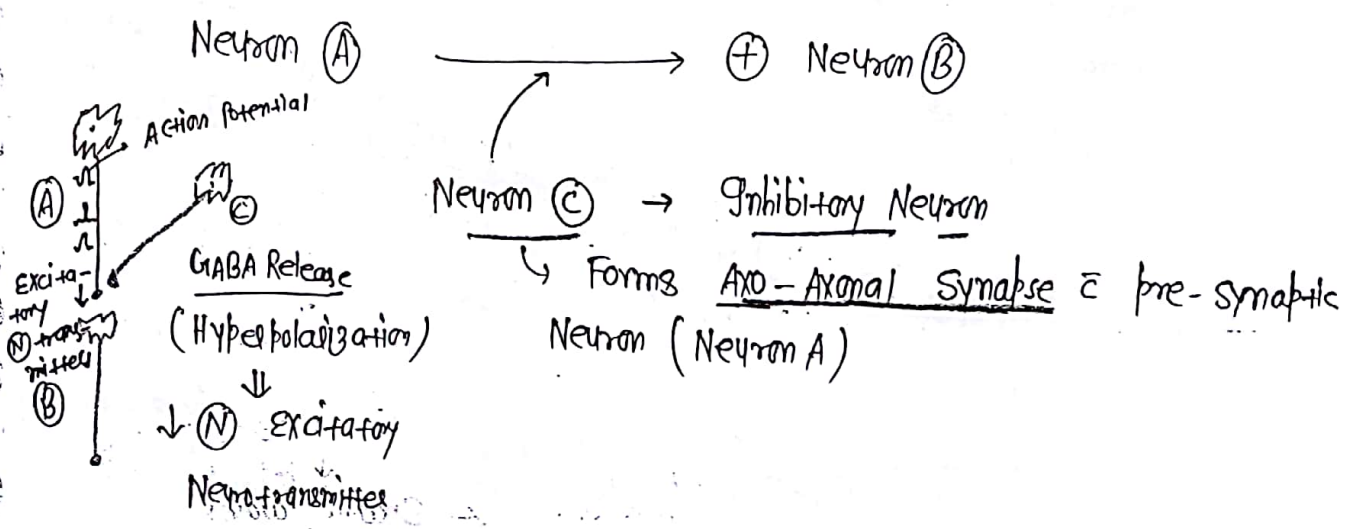
② STEVEN'S POWER LAW \Rightarrow Sensation level $\propto I^a$
(K, a \Rightarrow constant).
 $S = K I^a$

TYPES OF INHIBITION

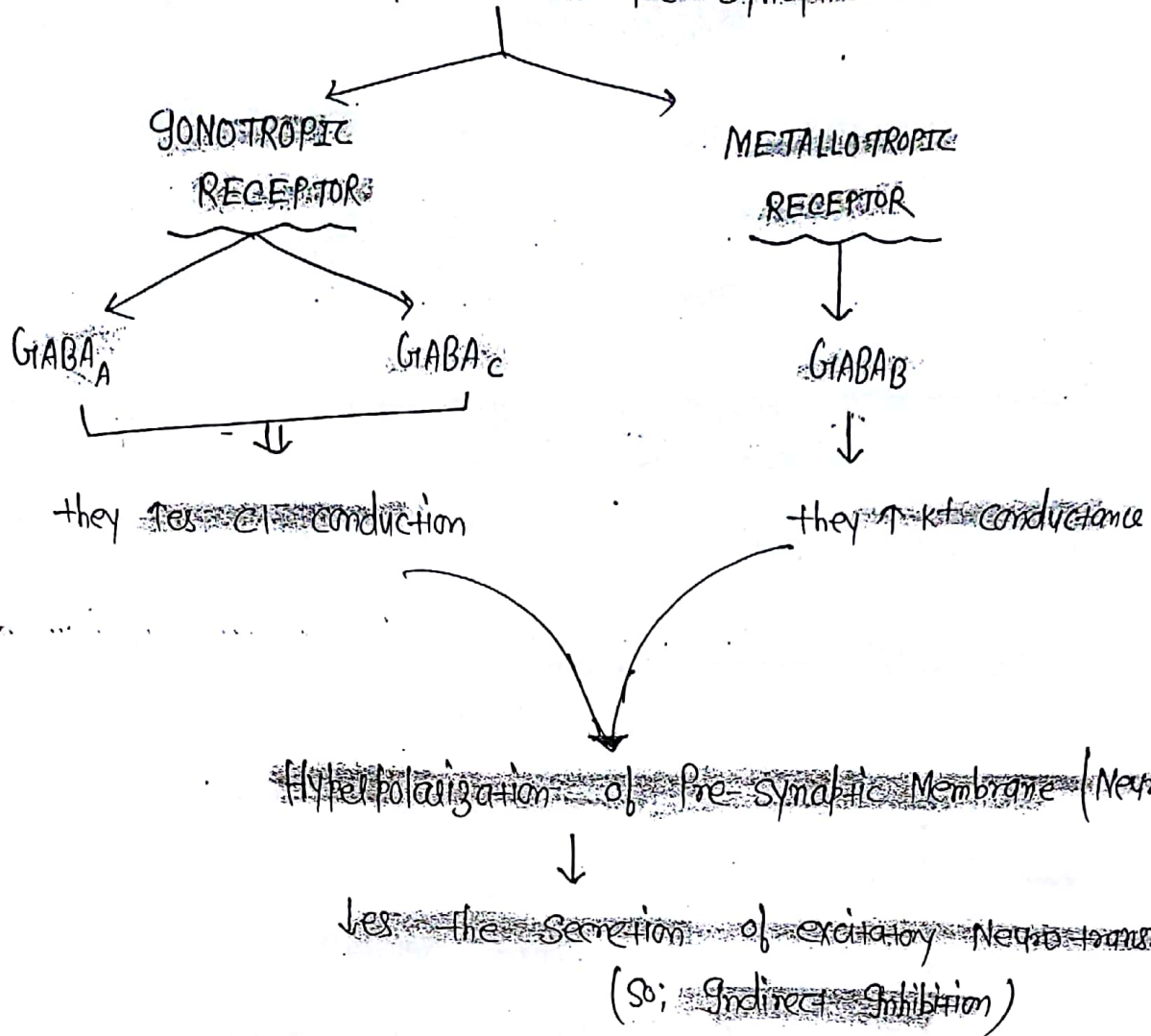
I. Direct / Post-synaptic Inhibition \Rightarrow



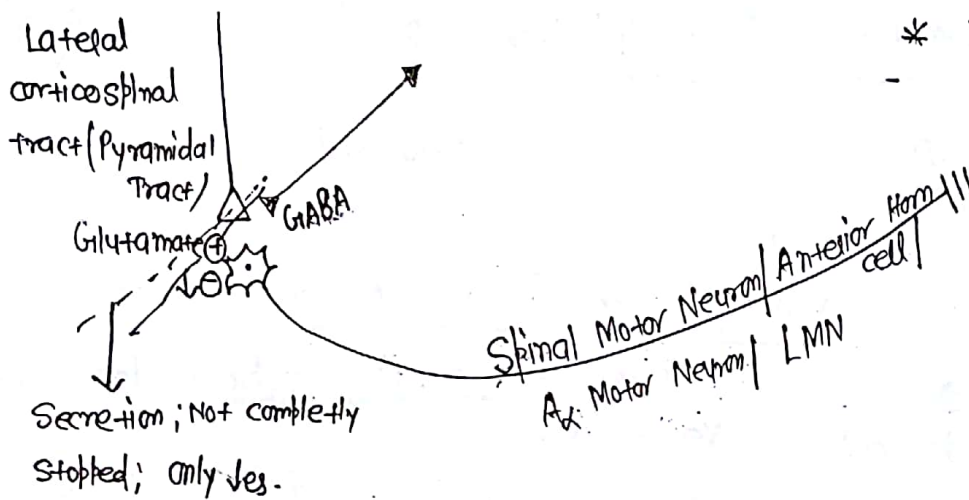
II. Pre-synaptic / Indirect Inhibition \Rightarrow



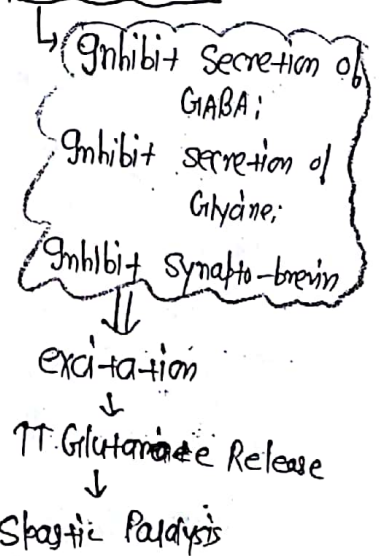
* GABA Receptor on Pre-synaptic Membrane



Advantage ⇒ Prevent Excessive Excitation of LMN
 ↓
 Fine & Well controlled Movement
 Fine and well controlled movement



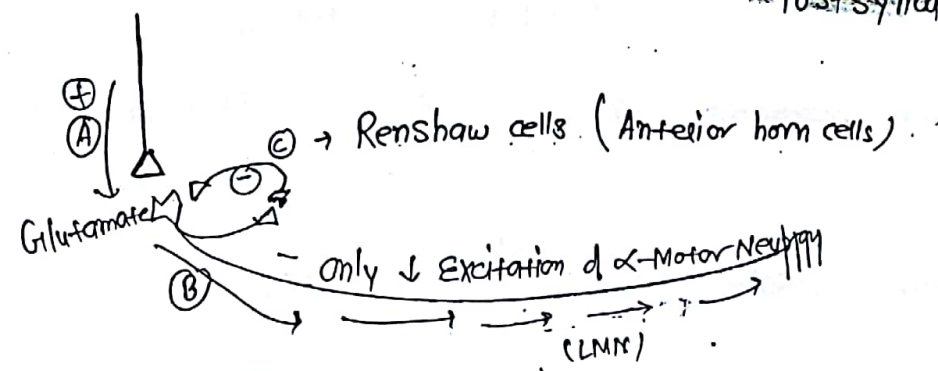
* Tetanus toxin



↓ + → ~~Hyperpolarization~~ of Pre-synap.

III. FEEDBACK INHIBITION (RENSHAW CELL INHIBITION) ⇒

↳ ~~Post synaptic type of inhibition~~

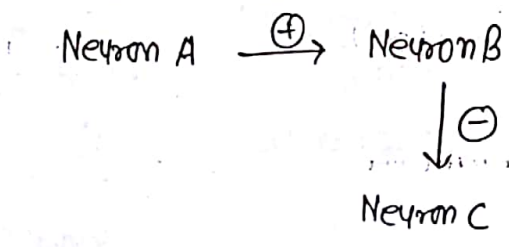


UMN → ⊕ LMN → Stimulate Muscle cells; but some impulse goes to Renshaw cell; which will inhibit UMN
↳ "Feedback Inhibition"

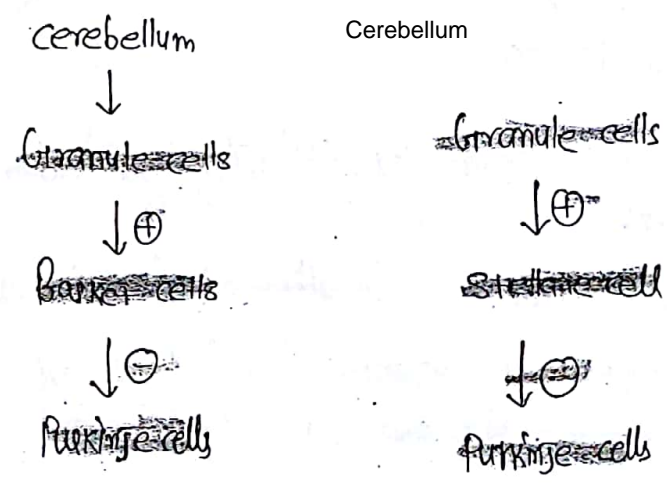
Advantage ⇒ Precise well control; well regulated Movement.
Prevent excessive excitement of LMN.

IV. FEED FORWARD INHIBITION ⇒

A neuron is connected through two pathway
~~A Neuron is connected through~~
~~two pathways; one excitatory~~
~~& one inhibitory~~
One: Excitatory and one Inhibitory



• typically seen in "Cerebellum"
Cerebellum



V. LATERAL INHIBITION \Rightarrow 2 Point Discrimination,

* if 2 points inhibit simultaneously

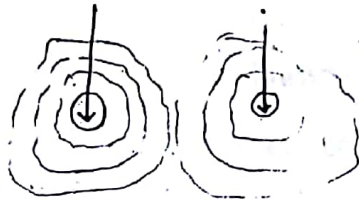


Inhibit surrounding (R)

* Min^m separable \rightarrow At finger tips (2mm)

So; Braille \rightarrow 2-5mm

- Max^m separable \rightarrow At back (65mm)

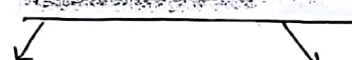


ASCENDING TRACTS (Sensory system)

Posterior column

- Fine Touch
- vibration
- conscious Proprioception
- Localization
- 2 point discrimination
- Stereognosis
- Ability to judge different degree of pressure

Spino-thalamic Tract



Lateral
Spino-thalamic
Tract (STT)
• Pain
• Temperature

Anterior
Spino-thalamic
Tract (STT)
• Crude Touch
• Itch
• Tickle
• Sexual sensation
• detection of Pressure (Barognosis)

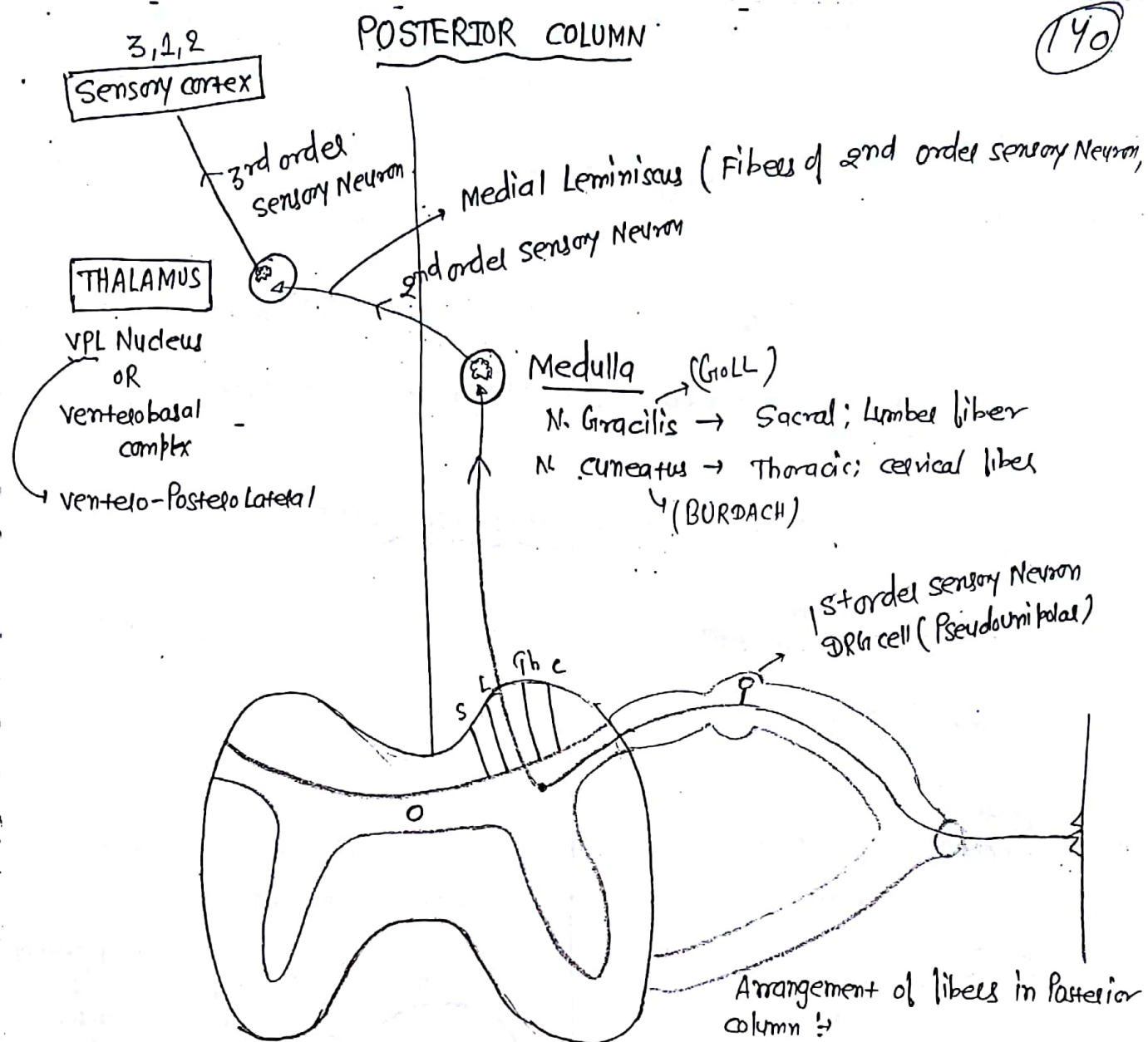
Spino-cerebellar Tract

• Unconscious
Proprioception

$\swarrow \searrow$
Dorsal Ventral
 $\downarrow \quad \downarrow$
Uncrossed crossed

Posterior column lesion; What will happen to Barognosis? (done by anterior STT)
(detection of "Pressure")
Graphesthesia (Localize the touch) is absent.

Proprioception is carried to spinal cord by A α sensory Neuron, while other sensation (Fine touch; Kinesthesia) are carried out by A β (type II) sensory Neurons.



Sensory cortex

- Posterior central Gyrus ;
- Area 3, 1, 2
- Sensory Homunculus (Physical Representation of Human body ; Located in Brain)

Grotesque Figure of Penfield & Rasmussen

Largest cortical Representation \Rightarrow Face including Lips

Smallest cortical Representation \Rightarrow Trunk & Back

CEREBRUM

6. Histological Layers \rightarrow I, II, III, IV, V, VI

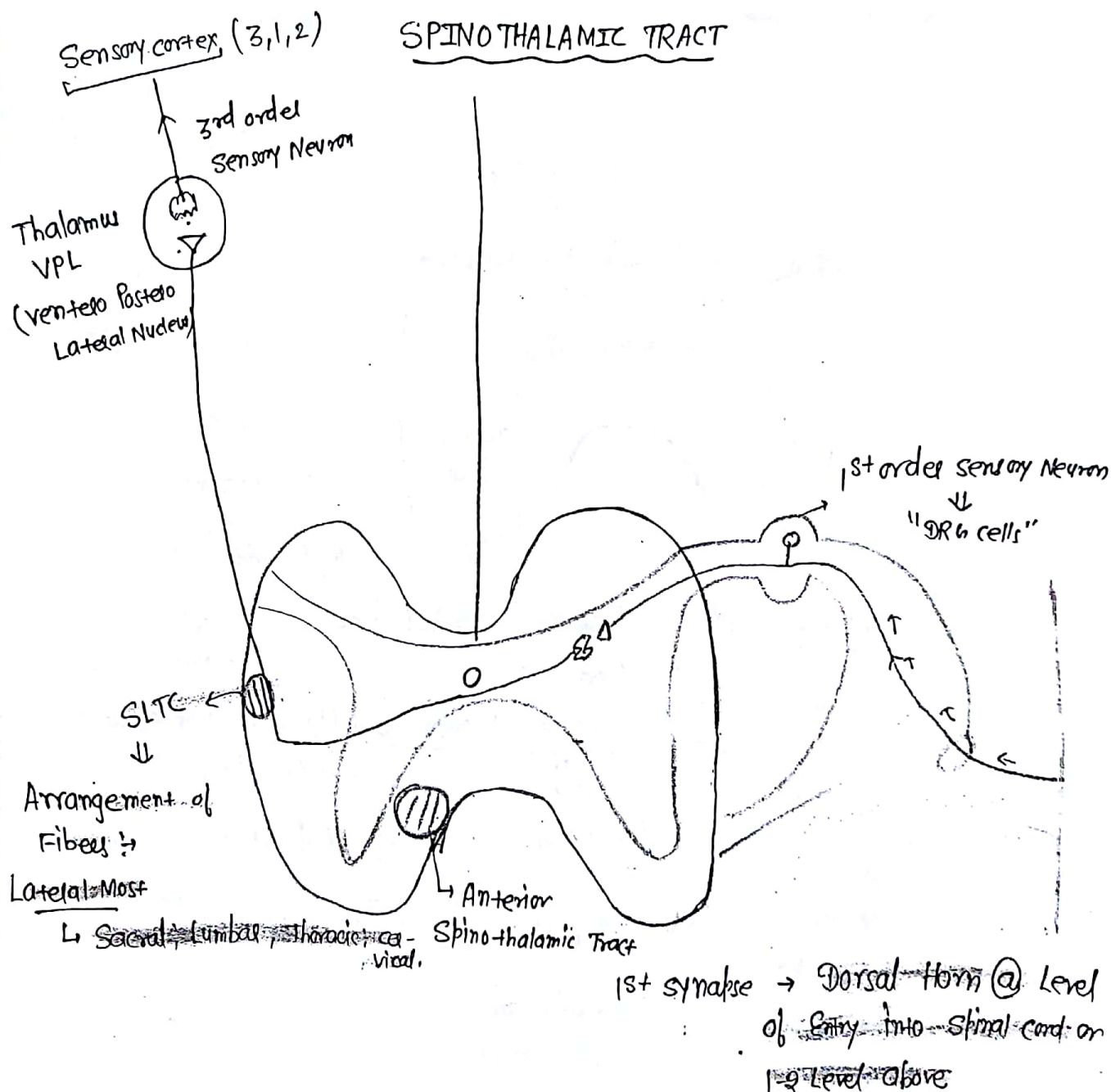
Bulk of Sensory Information.

Tract Specific for stereognosis \Rightarrow Fasciculus cuneatus

QO. Stereognosis Lost in lesion of \rightarrow (a) Fasciculus gracilis;
 \downarrow
Ability to identify an object by feeling it. (b) Fasciculus cuneatus;
~~(c) Cortex.~~

* Fasciculus gracilis \Rightarrow Fibres from Lower part of body

Fasciculus cuneatus \Rightarrow Fibres from upper part of body



* FAST PAIN PATHWAY / EPICRITIC PAIN

↳ evolved later

- Sharp pain; well localized
- Pricking sensation
- Stabbing sensation

- "Good Pain"
↓
(Responsible for Flexor
Withdrawal Reflex)

- Carried by → "A_δ"
- Felt in 0.1 sec
- Velocity → 12-30 m/sec
- Stimulus → Mechanical / thermal
- Neuro-transmitter → Glutamate
- Synapse - I/IV
(Lamina)

SLOW PAIN PATHWAY / PROTOPATHIC PAIN

↳ earlier evolved

Dull pain; diffuse pain

- Aching Pain
- Burning Pain
- Throbbing Pain
- Nauseous Pain

"Bad Pain"

↓

(Autonomic symptom a/w
Slow Pain Pathway)

"C"

Felt after 1 sec

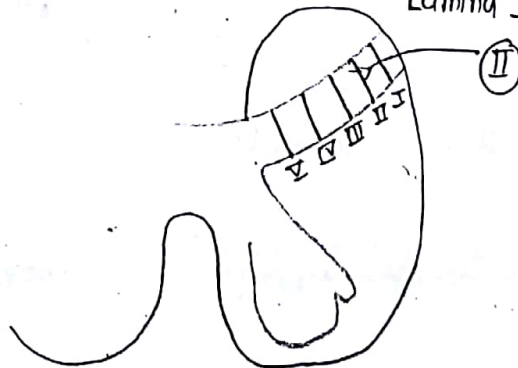
velocity → 0.5 m/sec

Chemical

Substance-P

- Posterior Horn divided into 5
Laminae
- (Whole grey Matter → 9 Laminae)

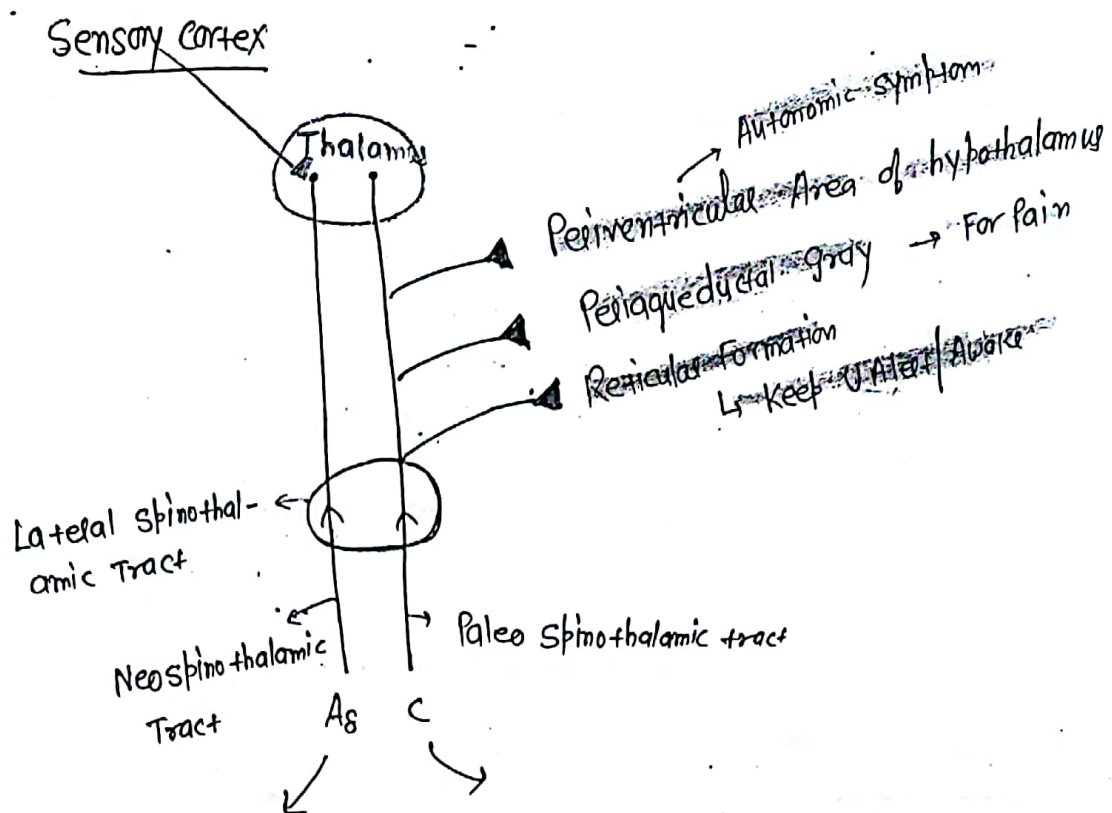
• Lamina II → Substantia Gelatinosa
of Rolando



A_δ Fibre → Klas "Neo-Spinothalamic Tract".

C Fibre → Klas "Paleo-Spinothalamic Tract" (Lateral Spinothalamic Tract)

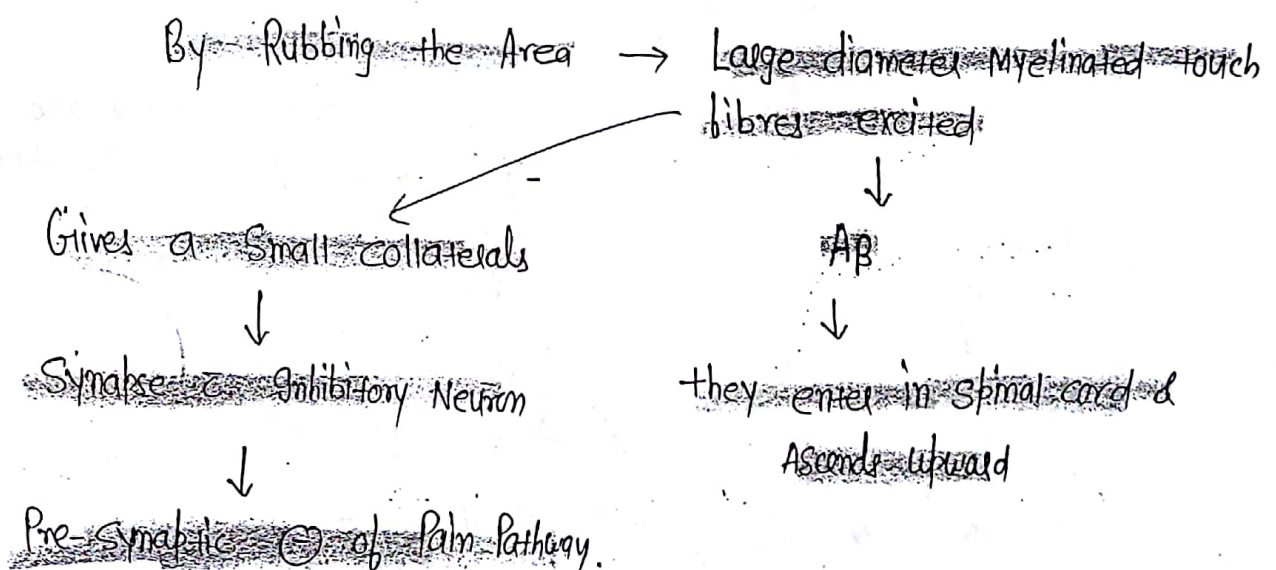
Both go to the thalamus
3rd order sensory neuron S. cortex.

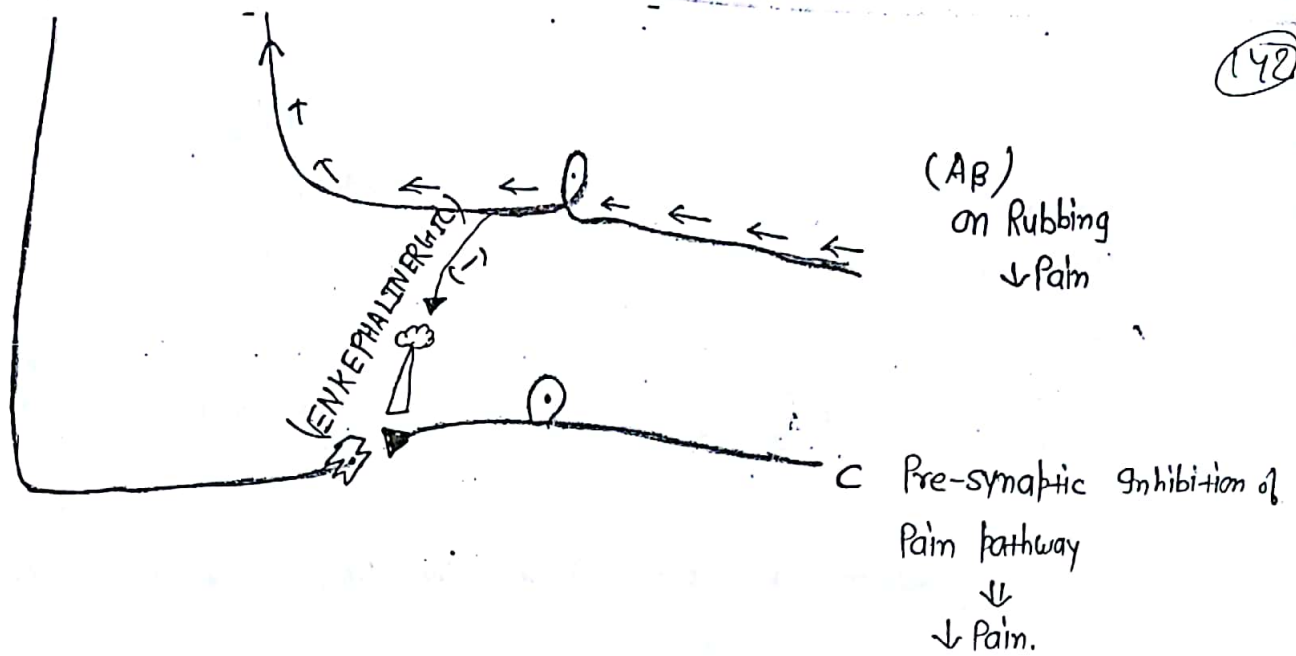


- Terminates @ Sensory cortex
- No branching
- Terminates @ Thalamus
- Gives branches (collaterals on the way)

• ENDOGENOUS ANALGESIA SYSTEM ; ⇒

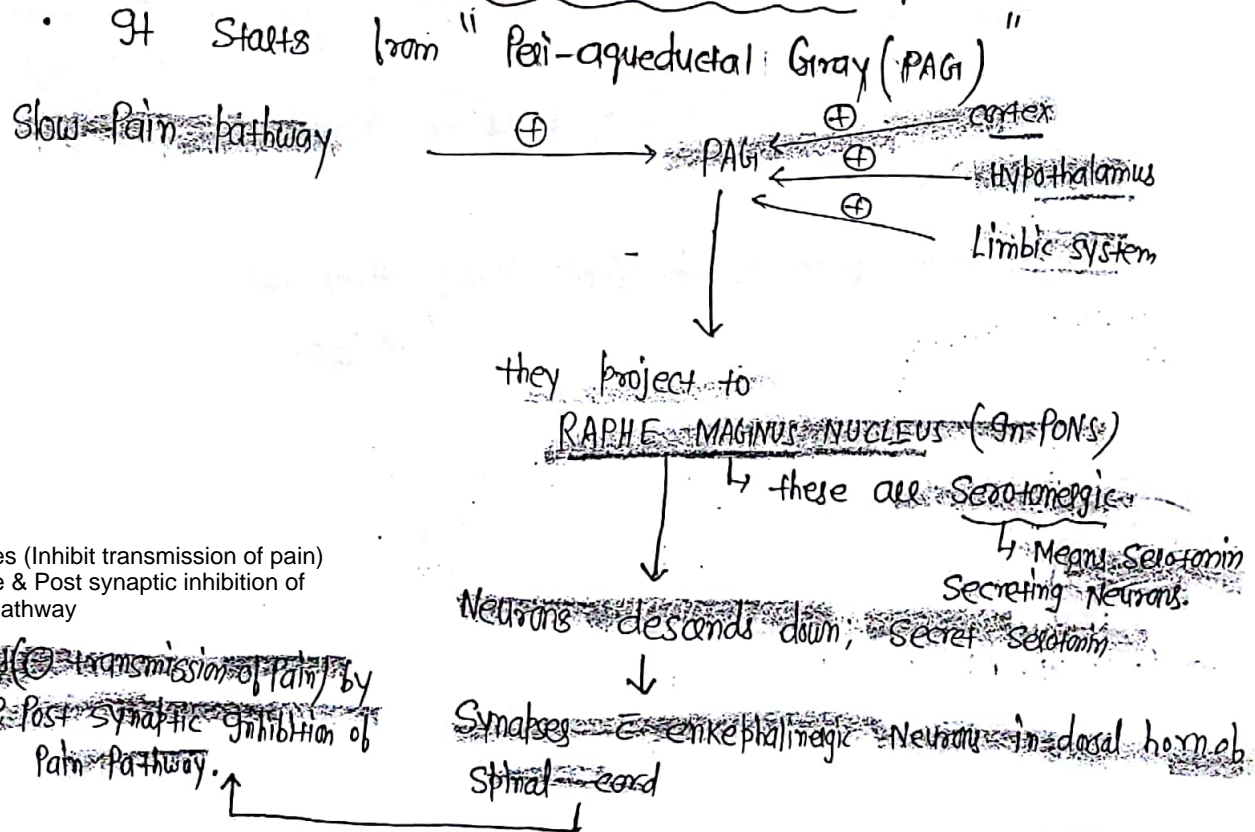
1. Gate control theory of MELZAC & WALL ; ⇒





TENS → Trans-cutaneous Electrical Nerve Stimulation;
based on Gate control theory of Melzack & Wall;
For Intractable Pain (cancer Pain) (Stimulate Aβ fiber)
↓
By Transcutaneous Electro

2. DESCENDING PAIN INHIBITION PATHWAY ⇒



De-cerebrate Rigidity

→ Severe extensor Rigidity

Neck
Upper Limb
Lower Limb

⇒ Extended

* Lesion @ Upper border of Pons

De-corticate Rigidity

→ Moderate Rigidity

Upper Limb → Flexion

Lower Limb → Extension

* Lesion above Mid brain

* In Decerebration → Lesion Above the Pons ; Both cortex & Midbrain Lost ;

↘ Cortico-Reticular fibres are destroyed

So; Inhibitory fibre for Medullary R.F. lost ; only excitatory fibre to Pontine R.F. from collaterals int.

Which develop → ↑↑ tone @ extension
Severe (extensor Rigidity)

* In Decortication → Lesion Above Midbrain ; Mid brain give some excitation
(only cortex is gone)

- Some amount of Inhibitory fibres to Medullary Reticular fibre will be intact

- excitatory fibre will be More ; but there will Moderate level of tone
(Moderate extensor Rigidity)

THALAMUS

143

It is a "Grand Sensory Relay Nuclei"

Sensory Relay Nuclei

Non-specific

Midline

Intra Laminar

Specific

- For Somatic Sensation

↳ Ventro Posterior Lateral

- For Visual Pathway

↳ LGN

- For Auditory Pathway

↳ MGN

- For Taste Pathway

↳ Ventro Posterior Medial

- For olfaction

↳ Mediodorsal thalamic

OR

Dorso Medial

* Motor Nucleus of Thalamus

- Ventro Anterior Nucleus

Ventro Lateral Nucleus

PAPEZ CIRCUIT - Involved in

Memory

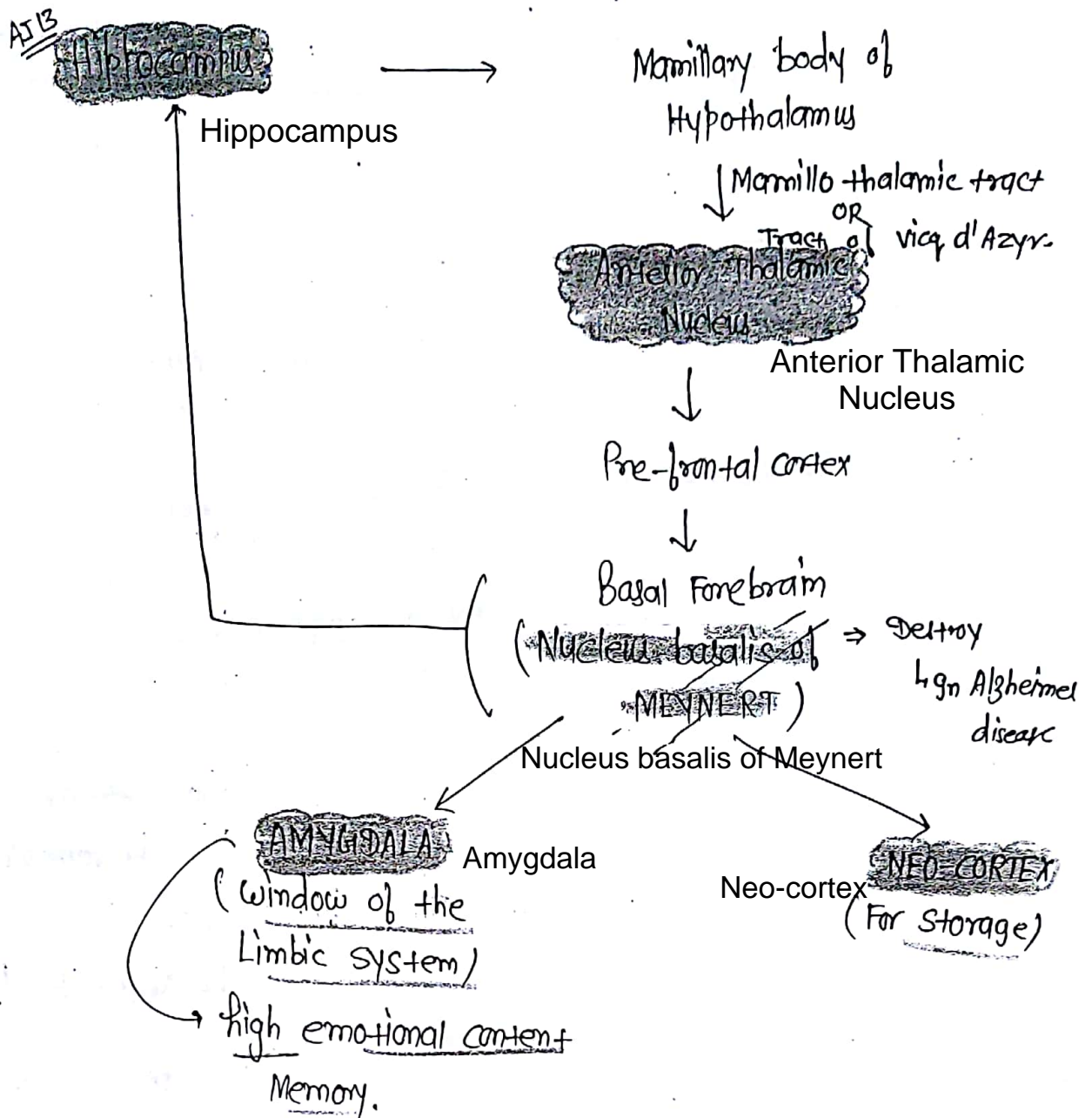
Learning

Emotion

↳ Interconnected closed circuit forms by various Nuclei of Limbic system.

↳ It starts from Hippocampus of Brain

↳ It connects Short term Memory → Long Term Memory.



A13 ⇒ Every thalamic Nuclei except → Retinacular Nuclei sends axon to different part of cortex.

REFLEXES

- Based on No. of synapses.

- ① Asynaptic Reflex ⇒ Axon Reflex
 - ↳ It is a part of Triple Response (Blunt Injury)
 - a) Red Reaction ⇒ b/c of Release of histamine
 - b) Flare Response ⇒ b/c of Axon Reflex
 - c) Wheel Response ⇒ d/c histamine & bradykinin

Axon Reflex \Rightarrow Blunt Injury over skin
 \downarrow
 excite the Pain fibre

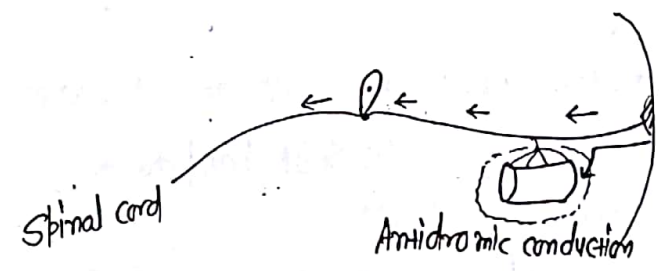
\downarrow
 Impulse goes to spinal cord; K/as "ORTHODROMIC CONDUCTION"

- These fibre also Receive branches from Blood vessels supplying these areas.
- Some fibres goes in "Antidromic conduction" of impulses to the blood vessels supplying the Area

\downarrow
 Arteriolar dilatation

\downarrow Spreading Redness

\downarrow K/as \Rightarrow "Flare Response"



② MONOSYNAPTIC REFLEX \Rightarrow Deep tendon Jerks;
 Stretch Reflex/ Myotatic Reflex.

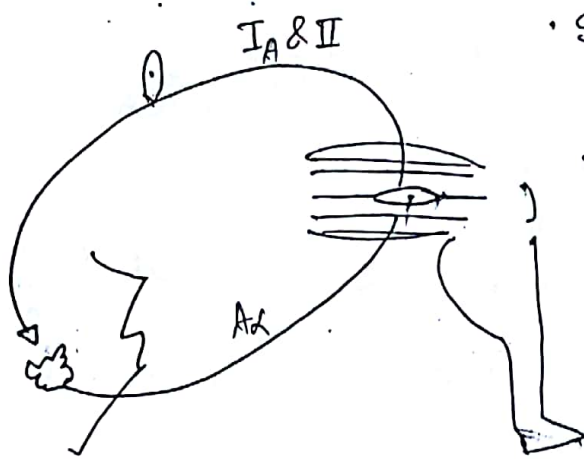
Knee Jerk - Strike over Patella Tendon.
 \downarrow
 Tendon Jolts

\downarrow
Increase in Muscle length

\downarrow Increase in Muscle length
 Muscle spindles get stretched

\downarrow
 Sensory fibres I_A & II enters into spinal cord

\downarrow
 In spinal cord synapse \bar{C} Ax fibres



- Stimulus for stretch Reflex
↳ ↑ in Muscle Length.
- Receptor for Reflex
↳ Muscle spindle
- Afferent fibres
↳ I_A & II
- Centre for stretch Reflex
↳ spinal cord
- Efferent fibres for Reflex
↳ A_x
- Response of Reflex
↳ Muscle contraction
- No. of Synapses
↳ 01 (one).

* During a stretch Reflex \Rightarrow Dynamic Response > Static
Nuclear bag (dynamic) \gg Nuclear bag (static)
& Nuclear chain fibre

* When a Muscle spindle is excited (\uparrow Muscle Length)
(\uparrow A_y discharge)

↓
Cause Muscle contraction

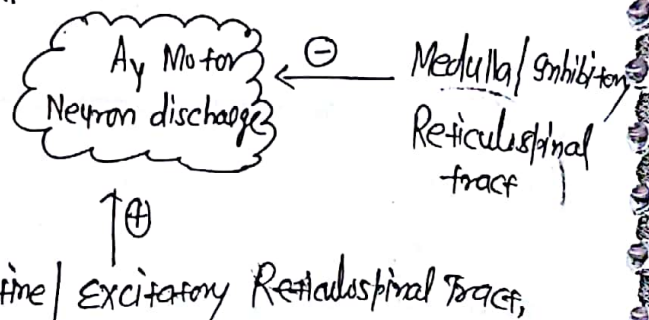
Q. Which tract control A_y Motor Neuron?

↓
Reticulo-Spinal Tract

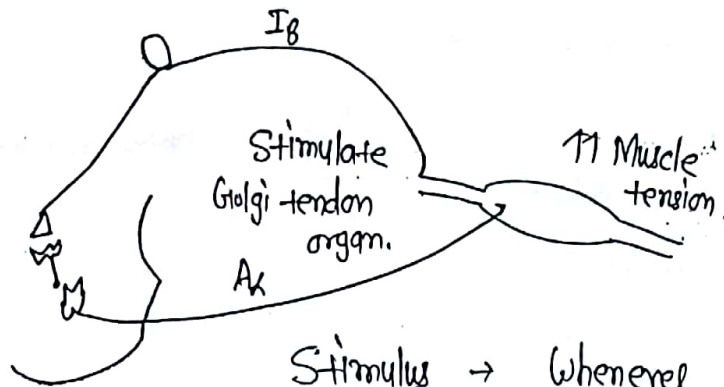
Q. Which tract control A_x Motor Neuron?

↓
Cortico-Spinal Tract

* A_y Motor Neurons are Not
Plentiful enough & Not Strong
enough to produce Muscle contraction
↓
So, they ~~are~~ Muscle tone



③ BISYNAPTIC REFLEX \Rightarrow Inverse stretch Reflex (Type 145) (Muscle Relaxation)



Stimulus \rightarrow Whenever there is ↑ in Muscle tension; it stimulates Golgi tendon organs (Receptors)

* There are 3-25 Muscle fibres | Golgi tendon organ.

* Golgi tendon organs act as "Muscle tension-detector".

↓
Nerve fibres Ib
↓
Synapse \bar{c} Inhibitory Neuron
↓
Inhibits Aα-Motor Neurons going to
particular Muscle

- * Stimulus \Rightarrow ↑↑ Muscle tension;
- * Receptor \Rightarrow Golgi tendon organ (G.T.O.);
- * Afferent Fibre \Rightarrow Ib !
- * Centre \Rightarrow Spinal cord;
- * Efferent Fibre \Rightarrow Aα
- * Response \Rightarrow Muscle Relaxation
- * No. of Synapse \Rightarrow 02 (Two) NEET 16

* When Muscle spindle excites \Rightarrow Muscle Contraction
(at Moderate stretch)

* When Golgi tendon organ excites \Rightarrow Muscle Relaxation
(on excessive stretch
OR
↑ Muscle tension) \rightarrow It has high threshold for stretch.

④ Polysynaptic Reflex \Rightarrow Most Reflexes

- Flexor Withdrawal Reflex
- crossed Extensor Reflex
- Micturition Reflex
- Defecation Reflex
- Sexual Reflex

} Higher centre control

DESCENDING TRACTS (MOTOR PATHWAYS)

Medial

- Control Axial Muscles
(Tone & Posture)



- Anterior corticospinal Tract
 - Vestibulo spinal Tract
 - Tecto-spinal Tract
 - Reticulo-spinal Tract
 - ↳ Pontine Reticulo-spinal Tract
 - ↳ Medullary Reticulo-spinal Tract
- $\left. \begin{array}{l} \text{Ax} \\ \text{Especially Lower} \\ \text{Limb Extension} \end{array} \right\}$
 $\left. \begin{array}{l} \text{Ay} \\ \text{Especially} \\ \text{Lower Limb Extension} \end{array} \right\}$

Lateral

- Control Distal Muscles
(Fine; Skilled Movements)



- Lateral cortico-spinal Tract
(Pyramidal Tract)
 - Rubrospinal Tract
(Alternate Pathway)
(Extrapyramidal Tract; Similar acting Pyramidal Tract)
- $\left. \begin{array}{l} \text{Ax} \\ \text{Especially} \\ \text{Upper Limb} \\ \text{Flexion} \end{array} \right\}$

* CORTICOSPINAL TRACT

Origin \rightarrow ① Primary Motor cortex \Rightarrow Contributes 30% fibres of corticospinal Tract;

\rightarrow Located in Pre-central Gyrus: Area 4*

Motor Homunculus

(19)

↳ Largest cortical Representation*

↳ More complicated movement.

↳ Largest - Muscle of Vocalization; (Maxⁿ)
Muscle of Mastication; (2nd Maxⁿ)
Muscle of Thumb

Smallest cortical Representation - Muscle of Trunk/Back.

② Pre-Motor | Supplementary Motor Area ⇒ Area 6⁺⁺
↳ contributes 30% of the fibres.

③ Sensory cortex ⇒ contributes 40% of the fibres
(so, there are 40% sensory fibres in corticospinal tract).
↳ Area 3, 1, 2

I

II

III

IV

V

VI

Histological Layer of
Cerebrum.

→ bulk of incoming sensory information (Layer IV)

→ Motor output (Majority of Motor fibre).

Pyramidal cells of
BETZ

Betz cells

↓

Large (16 μ m) Myelinated fibre
originated from "Giant Pyramidal
cells".

- Found in Primary Motor cortex.

* CORTICO - SPINAL TRACT - COURSE

Fibres from different Areas of cortex

Pass through Internal cortex

Anterior 2/3rd of Post. Limb & Genu

Reach to Medulla

80% fibre cross over to opposite Side (Pyramidal) → Motor decussation

80%

Medulla

Motor Decussation (Pyramids) → Motor

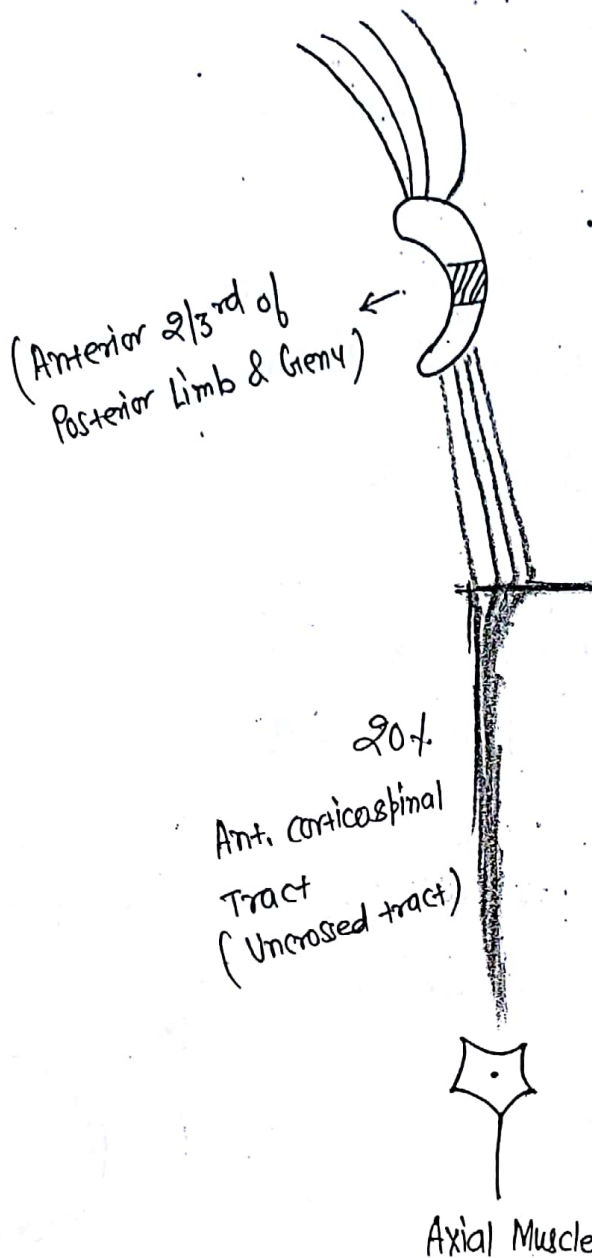
Lateral corticospinal Tract (Pyramidal tract) → crossed tract



Distal Muscle

(Fine, skilled Movement)

Form Lateral corticospinal tract (Pyramidal tract)



20% Fibre ; Which Not cross

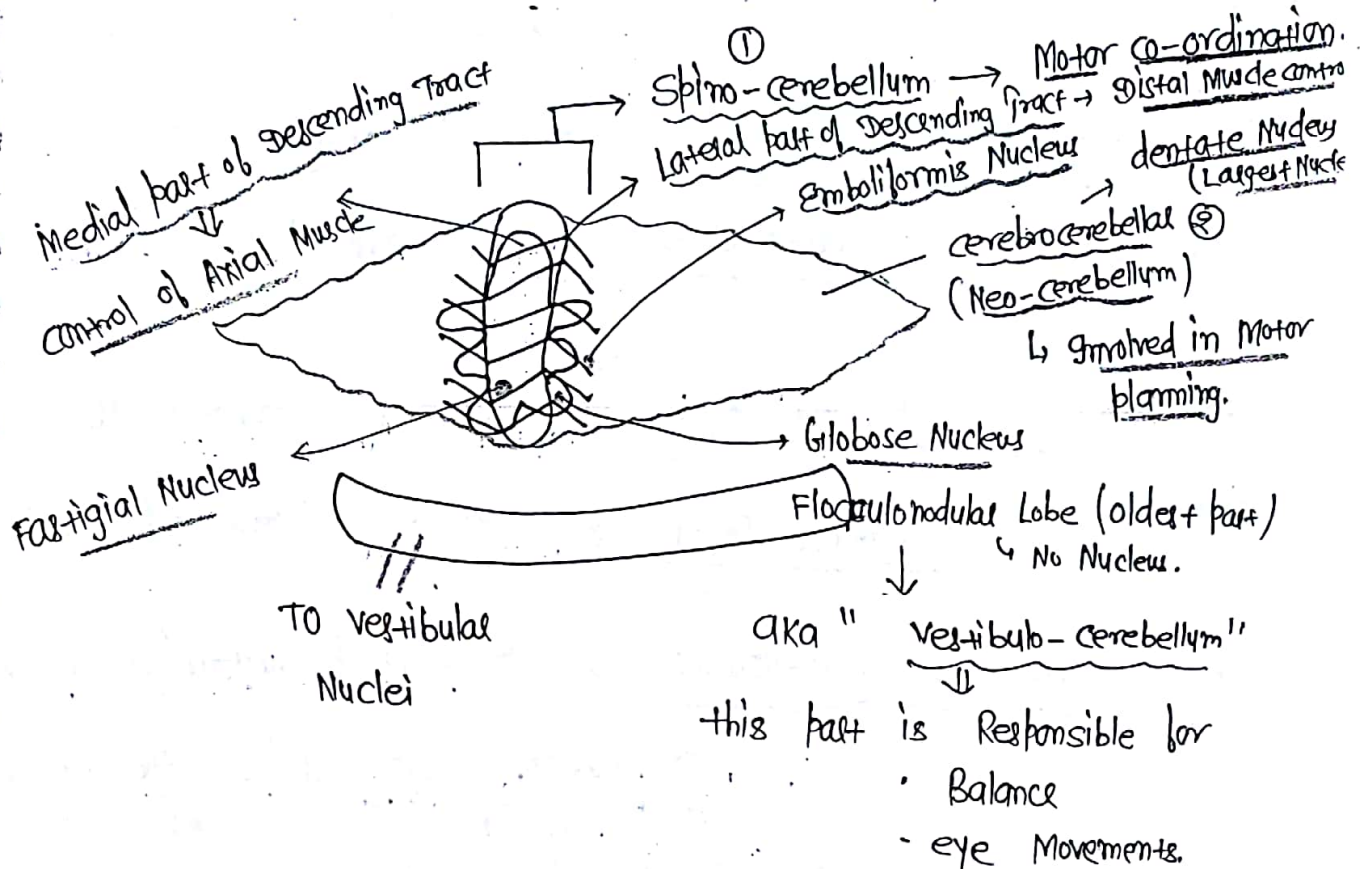
Form Anterior corticospinal Tract (Uncrossed)

For Axial Muscles.

CEREBELLUM

(147)

- 3 parts :
- 4 Nucleus (4 pair) ⇒ ~~Collection of Gray Matter~~
Collection of Gray Matters
- 5 cells ;



Q. Q. Most imp. function of cerebellum →
a) Motor co-ordination;
b) Motor planning.

* 4 Nucleus →
Medial to lateral

① Fastigial Nucleus → Medial part of Spinocerebellum

② Globose Nucleus } Lateral "

③ Emboliformis Nucleus }

④ Dentate Nucleus → Neo-cerebellum
↳ Largest Nucleus.

- * S-cells →
- i> Granule cells → excitatory;
 - ii> Basket cells
 - iii> Stellate cells
 - iv> Golgi cells
 - v> Purkinje cells
- } → Inhibitory;
- ↳ Largest cells.

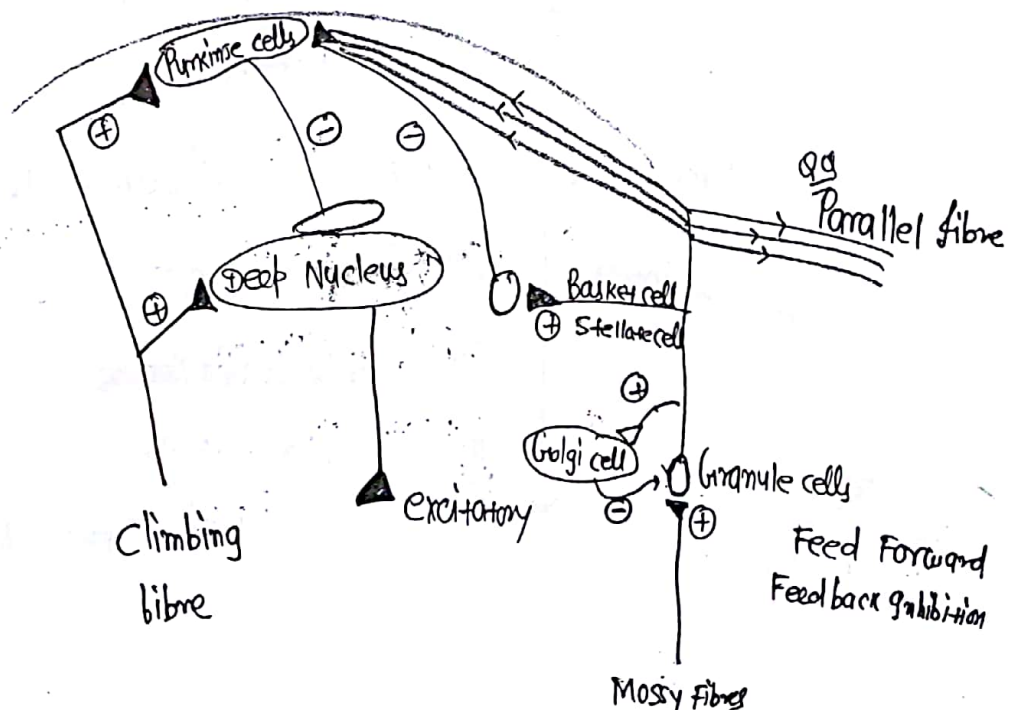
* Cerebellar cortex arranged in three layers ⇒

- ① External Molecular Layer ⇒ contains Basket cells & stellate cells;
- ② Middle Purkinje cells ⇒ contains Purkinje cells;
- ③ Inner Granular Layer ⇒ contains Granule cells & Golgi cells

* OUTPUT OF CEREBELLUM ⇒ From deep Nucleus (excitatory output)

↳ Purkinje cells inhibit the output of deep Nuclei.

* Output of cerebellar cortex → Purkinje cells.



INPUT INTO CEREBELLUM → via 2 types of fibre

(148)

CLIMBING FIBRE

- Strong excitatory input;
- Formed by fibres of the Olivocerebellar tract
(It brings proprioceptive impulses from whole body)

* Climbing fibre → ⊕ Deep Nucleus

So, it is 1st excitatory then it is also give ⊕ stimulus to Purkinje cells; so, later on it is inhibitory.

* Climbing fibres bring information only from "Inferior olivary Nucleus"

MOSSY FIBRES → They synapse ⊖ Granule cells

Parallel fibres travel into cortex

Synapse ⊖ Multiple Purkinje cells

Inhibit deep Nucleus

* Granule cells excite a Golgi cells

Inhibits

MOSSY FIBRES

- Weak excitatory input
- Rest all fibres.

- * ROMBERG SIGN - ⊕ In posterior column lesion
 a/k/a ⇒ "Sensory Ataxia"
- ↳ When eye closes → Ataxia
 open → stable (good balance)

BASAL GANGLIA

- Involve in Motor Planning
- Co-ordination of Autonomic and Associat. Movement

↓
 ↳ Swinging of Arms while walking
 Facial expression while talking
 ↓
 Cycling.

To Kill a Fly (Insect)
 ↓ We Need
 Cerebellum control

⇓
 Rate
 Range
 Force
 direction } of Voluntary Movement

Caudate Nucleus
 ↓
 Major Role in cognitive control
 of Motor activity.

components

- 1. Caudate Nucleus
- 2. Putamen

↳ Receives Most of the afferent
 Input coming to the basal
 Ganglia.

Striatum

95% of Neuron Secrete ⇒ GABA
 5% of Neuron Secrete ⇒ Ach
 Somatostatin

3. Globus Pallidus → In Athetosis; Mainly affected part
 ↳ condⁿ in which abnormal muscle contraction causes involuntary writhing movements.
 External segment → Internal segment
 ↓ ↓
 GABA Secrete GABA Secrete

4. Substantia Nigra → Principal output Nuclei i.e. the efferent arises from there
 Substantia Nigra → Substantia Nigra → destroy in Parkinsonism.
 Pars Reticularis Pars compacta
 ↓ ↓
 GABA Release Dopamine Release

5. Subthalamic Nucleus of Lewis → it affected "BALLISM" may cause
 ↳ Release Glutamate ⇒ Excitatory Neurotransmitter

PATHWAYS ⇒

- ① Striato Pallidal GABAergic Pathway;
- ② Striato Nigral GABAergic Pathway;
- ③ Intra-striatal cholinergic Pathway;
- ④ Nigro-striatal Dopaminergic Pathway;
- ⑤ Subthalamic Nucleus of Lewis

Glutamate → Globus Pallidus external segment,
 Glutamate → Globus Pallidus internal segment.

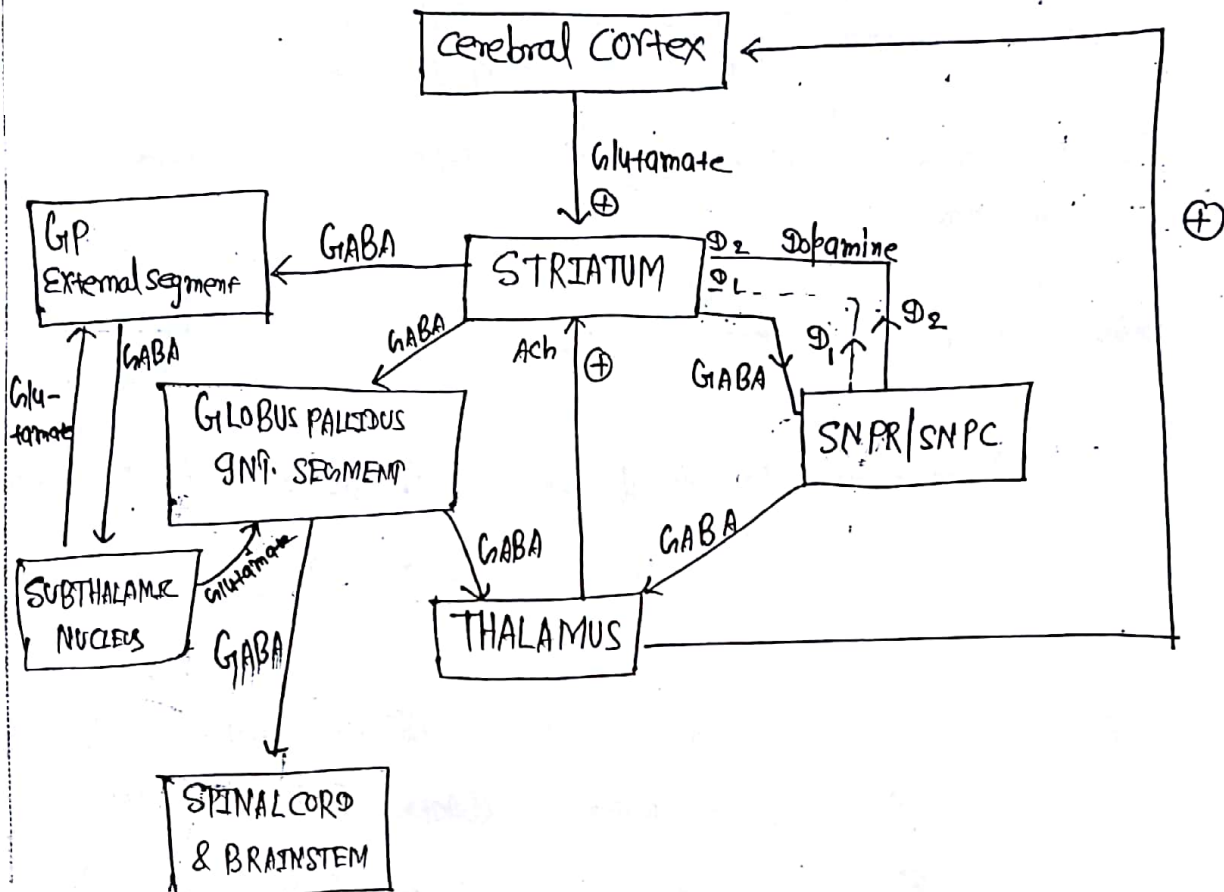
* In Huntington chorea ⇒ Mainly "striatum" part involved
 (Caudate Nucleus; Putamen)
 ↳ Loss of Intra-striatal GABAergic & cholinergic Neurons occurs.
 ↳ Both Cholinergic & GABAergic Neuron Involved.

* Dopamine Receptor $\xrightarrow{\oplus \text{ in}}$ Striatum

$D_1 \rightarrow$ Excitatory

$D_2 \rightarrow$ Inhibitory

* CONNECTIONS \Rightarrow



POSTURAL REFLEX

POSTURE \Rightarrow Static position of Any part of the body.

• This Reflex helps to Maintain posture.

Mainly of Four types \Rightarrow i) Spinal; ii) Medullary; iii) Mid brain; iv) cortical.

A. SPINAL POSTURAL REFLEX \Rightarrow 1. Stretch Reflex (Basic Postural Reflex) ;
 \rightarrow Stimulus of Stretch Reflex is Passive stretch

2. Inverse spinal Reflex ;

3. ⊕ve Supporting Reaction ; like "Magnet Reflex"



Receptor \rightarrow Touch (R) on foot pad



Extension of Limb.

4. ⊖ve Supporting Reaction : if foot pad contact move from ground \rightarrow Flexion of Limb.



5. Standing ;

6. Walking ;

7. Galloping ;

B. MEDULLARY POSTURAL REFLEX \Rightarrow 1. TONIC NECK REFLEXES \rightarrow

changes in posture ; d/t Movement of Neck ;

Receptor \Rightarrow Neck Proprioceptors.

- * Neck flexion \rightarrow Flexion of Forelimb
- \rightarrow extension of Hindlimb.
- * Neck extension \rightarrow extension of Forelimb
- \rightarrow Flexion of Hindlimb.

2. Vestibular Labyrinthine Reflex →

keeps the head horizontal w.r.t. ground

Receptors → Otoliths (in semi-circular canal).

C. MID BRAIN REFLEXES →

- All Righting Reflex — Except — Visual Righting Reflex
(correction of Body Posture) → centre ⊕ in cortex.

eg → Head on Body Righting Reflex • Vestibular Righting Reflex
Body on Body Righting Reflex. → centre ⊕ in Medulla.

D. CORTICAL REFLEXES → Hopping Reflex Placement Reflex.

* CSF

→ 150 mL

→ Daily Secretion → 550 mL/day / 0.38 mL/day

→ Secreted by "choroid plexus;"

→ circulate by "subarachnoid space" & Absorb by "Arachnoid villi."

→ It is secreted & Absorb → 3.7 times per day
(once every 6 hr)

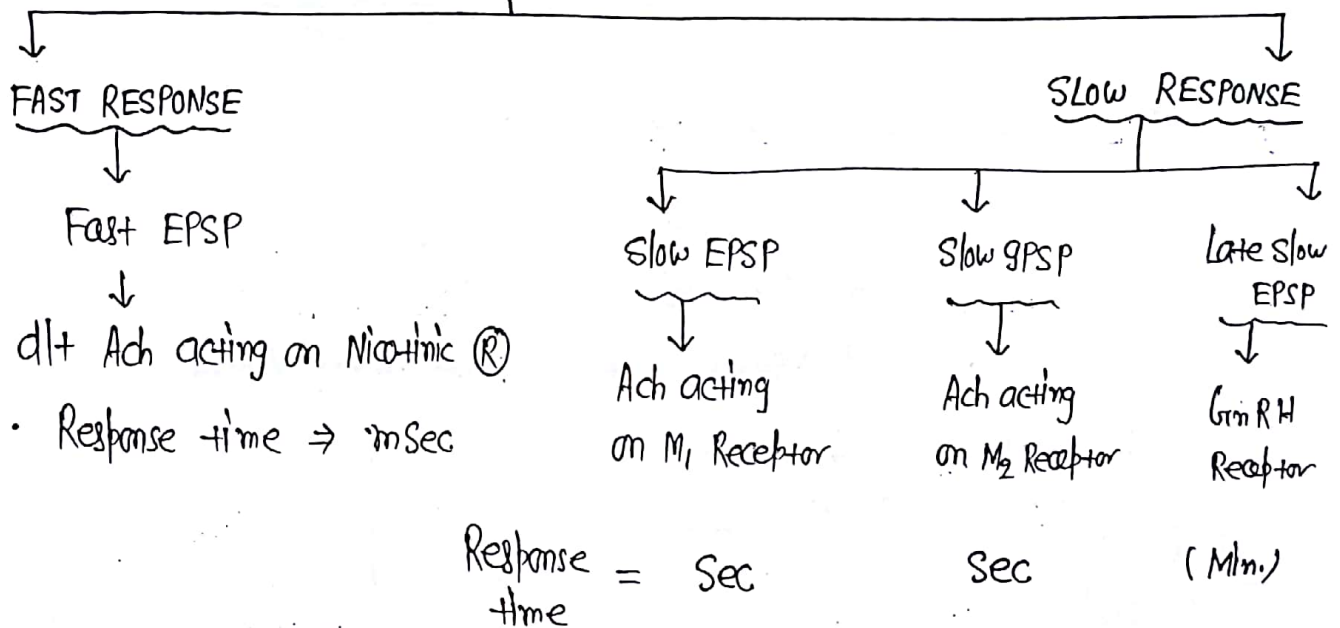
→ (N) CSF pressure → 70-180 mm H₂O
8-12 mm of Hg

- * Rate of CSF Secretion \Rightarrow Independent of CSF Pressure (15.7)
- * Rate of CSF Absorption \Rightarrow Dependent on CSF Pressure.

* At CSF Pressure

$112 \text{ mm H}_2\text{O} \Rightarrow \text{Secretion} = \text{Absorption}$
 $> 112 \text{ mm H}_2\text{O} \Rightarrow \text{Absorption} \uparrow$
 $< 112 \text{ mm H}_2\text{O} \Rightarrow \text{Absorption} \downarrow$
 $< 68 \text{ mm H}_2\text{O} \Rightarrow \text{No Absorption.}$

* TRANSMISSION GN AUTONOMIC GIANGLION



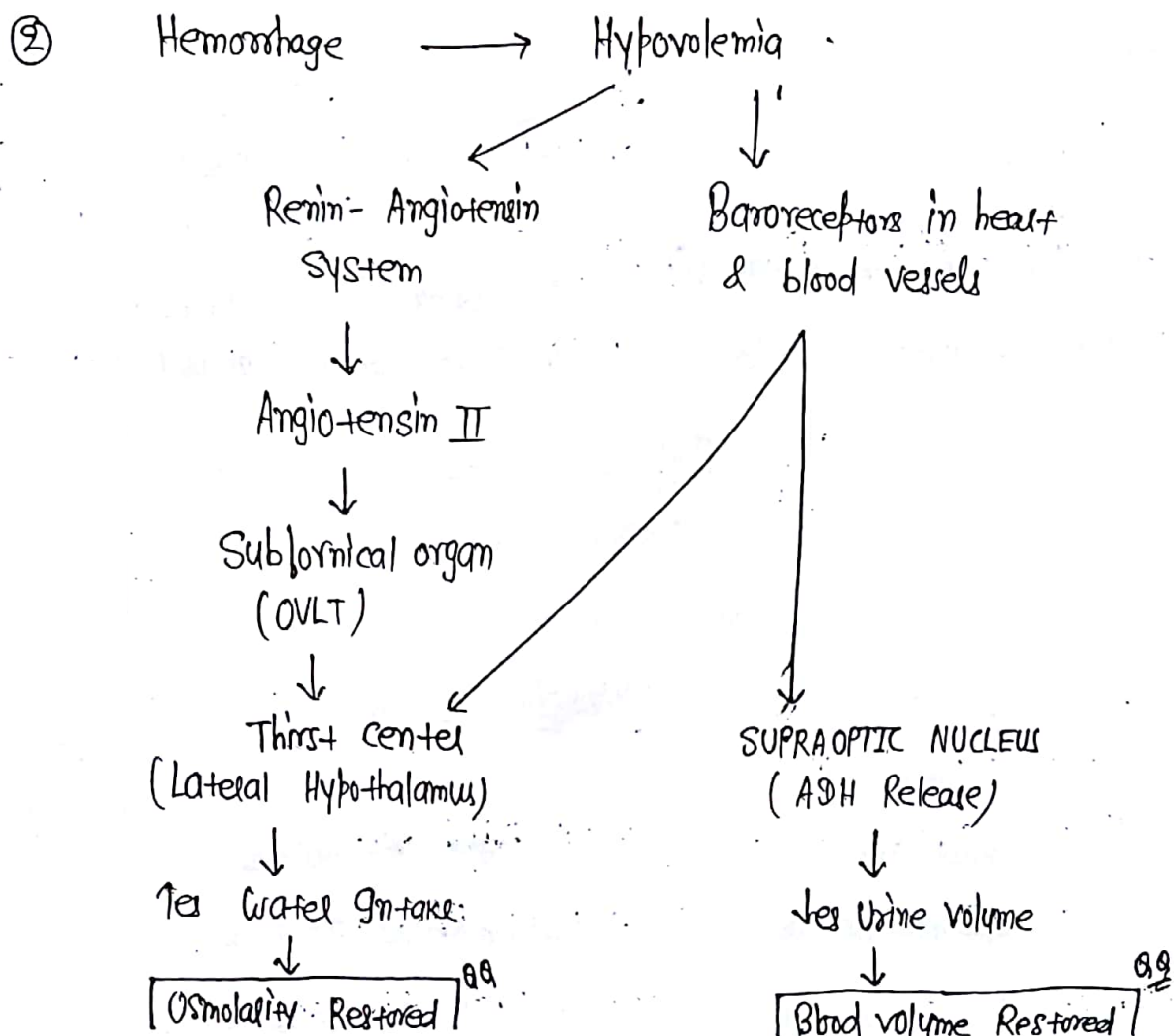
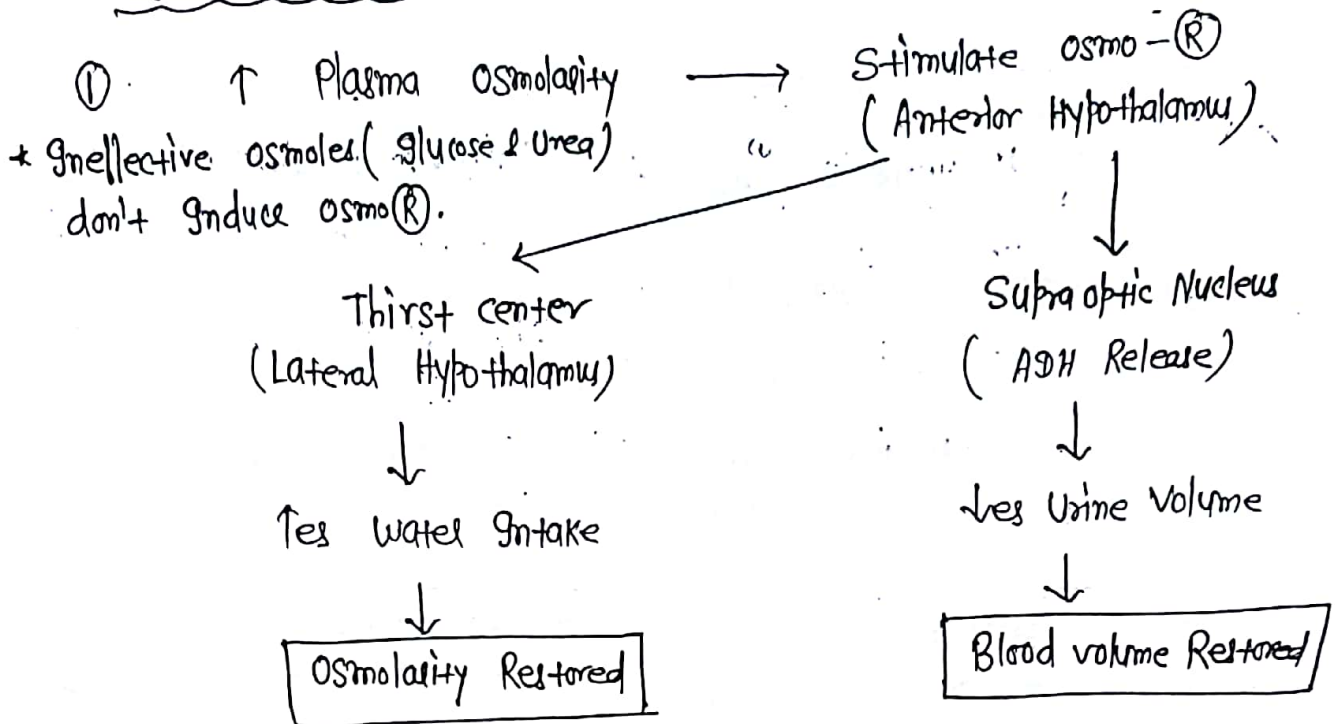
HYPOTHALAMUS

\rightarrow Vegetative Brain;

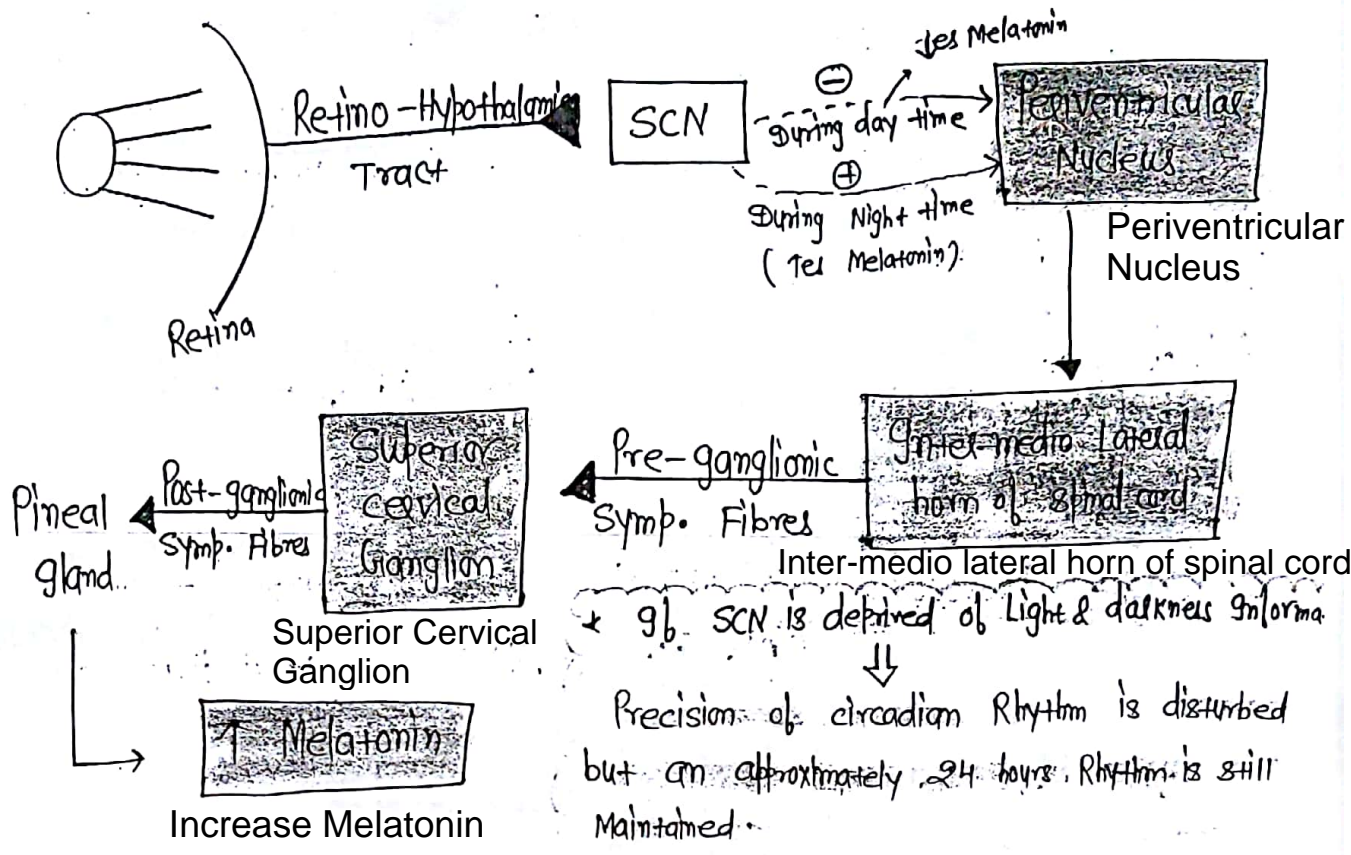
Hunger centre \rightarrow Lateral Hypothalamus
 Satiety centre \rightarrow Ventromedial Hypothalamus
 Thirst centre \rightarrow Lateral Superior Hypothalamus

Circadian Rhythms → Suprachiasmatic Nucleus

* Regulation of Thirst ⇒



* Circadian Rhythm - Supra-chiasmatic Nucleus is involved,
believed to contain the "Biological clock"



* RAGE CENTRE → Lateral Hypothalamus (Aggressive)

* REWARD CENTRE (Flaccid) → Medial Forebrain bundle
Nucleus Accumbens (Drug Addiction)
Ventral-medial hypothalamus.

* PUNISHMENT CENTRE → Posterior Hypothalamus & Dorsal Mid-brain;

* AVERSIVE RESPONSE → Learned Negative/Undesired Reaction to an Unpleasant event.
↓
Pei-aqueductal - Gray (PAG)

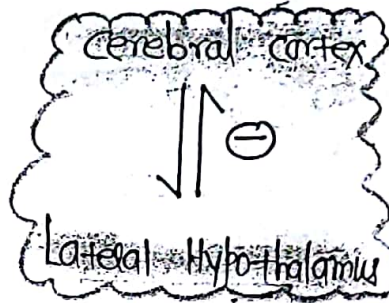
* SELF STIMULATION EXPERIMENT → Experiment: Animal kept in a cage.
↓ electrodes are placed in different Areas of brain & they are connected to a Lever; when he presses the Lever → Response.

* It is Most effective ; if electrode is placed at Medial Forebrain Bundle

* SHAM RAGE \Rightarrow Sham Means False.

\Downarrow
Seen in Decorticate Animals
 \Downarrow

Animals whose whole Cerebral cortex has been removed.



* Slight provocation to Animal \longrightarrow Goes into Rage
(B/c No Inhibition to Lateral Hypothalamus).

* This Rage is Not Goal directed **

* Sexual Responses \Rightarrow Anterior Most & Posterior Most portion of Hypothalamus
Anterior Hypothalamus (especially Medial Pre-optic Nucleus) is More Important.

* In Males Additional Area \Rightarrow Piriform cortex.

* TEMPERATURE REGULATION (PRE-OPTIC REGION)

\downarrow
Posterior Hypothalamus
(Heat gain centre)

\downarrow
Response to cold (winter)

i) \uparrow Sympathetic discharge

\hookrightarrow Peripheral Vaso-constriction

\downarrow
Anterior Hypothalamus
Including Pre-optic Nucleus
(Heat Loss centre)

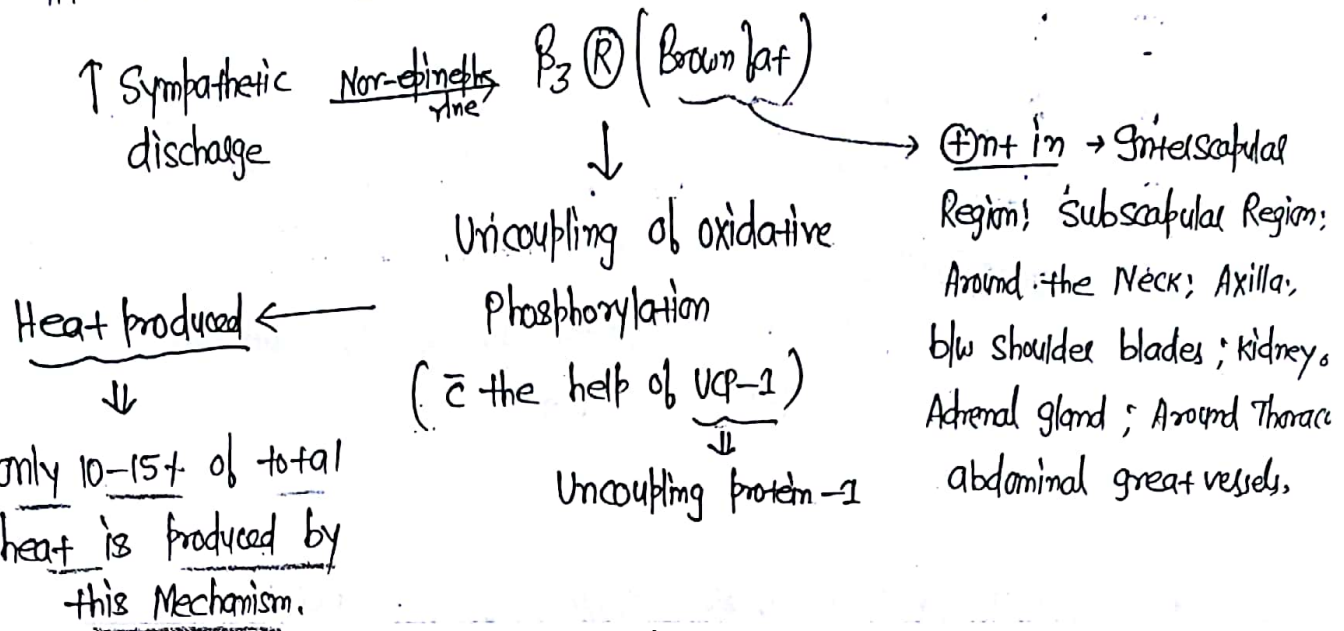
\downarrow
Response to warm (Summer)

i) Peripheral Vasodilation;

ii) Sweating

(Sympathetic cholinergic fibres)

Posterior Hypothalamus
ii) Non-Shivering thermogenesis



iii) Shivering

kk Radiation is Major Mech^m for Heat gain & Heat loss.

* Dominant / Categorical Hemisphere ⇒ Left hemisphere is k/as "Dominant hemisphere"

In 95% Person → Left side

• B/c Wernicke's & Broca's Area is More developed in Left side → "calculation"

So; if Left hemisphere damage ⇒ Acalculia.

* Non-dominant / Visuo-spatial Hemisphere ⇒ Rt. side

Involve in Fine Art; Creativity; Dance; Music

Rt. Inferior temporal Lobe ⇒ Recognition of Faces

Loss → PROSOPAGNOSIA / FACE BLINDNESS

Q.Q.

Temporal Lobe functions are all except \Rightarrow

- a) Memory;
- b) Hearing;
- c) Behaviour \rightarrow Ant. Most part of Frontal & temporal Lobe (Mainly Motivation)
- d) Spatial orientation
 - \hookrightarrow Completely Parietal Lobe function.
 - \hookrightarrow GPS of Brain*

*

CIRCUMVENTRICULAR ORGAN (OUTSIDE BBB) \Rightarrow

Structure in the brain that are characterized by their extensive vasculature & Lack of Normal BBB.

- ① OVLT (Organum Vasculosum of Lamina terminalis);
- ② S.F.O. (Subfornical organ);
- ③ Median eminence;
- ④ Area - Postrema
 - $\xrightarrow{\text{control}}$ CTZ (chemoreceptor trigger zone)
 - \rightarrow CVS
 - \rightarrow Medullary structures in the brain that controls vomiting.
- ⑤ Posterior Pituitary (Neurohypophysis)

EEG (ELECTROENCEPHALOGRAPHY)

Delta wave (S-wave) \Rightarrow Origin = cortex;

\hookrightarrow Occur independent of activity in lower Areas.

NREM

* K/as "Synchronized sleep"

OR

"Quiet sleep"

OR

"Orthodox sleep". ag

Events \Rightarrow

- SOMNAMBULISM (Night walking)
- SOMNILOQUY (Sleep talking)
- NOCTURNAL ENURESIS
- BRUXISM (Teeth grinding)
- NIGHT TERRORS (Pavor Nocturnus)

\rightarrow NREM
(III & IV)

REM

• Spontaneous Awakening occurs in REM sleep.

• This is period of Autonomic Instability

HR
BP
RR] Irregular.

* ~~P-G-O~~ Spikes all seen
(Ponto-geniculo-occipito)

PONS \Rightarrow ~~P-G-O~~ on cells

• Ach Release

Events \Rightarrow NIGHTMARES ;

• NOCTURNAL PENILE TUMESCENCE

• NARCOLEPSY

(Excessive day-time sleep)

\rightarrow a/w cataplexy (loss in muscle tone).

Hypnagogic hallucination

Sleep paralysis

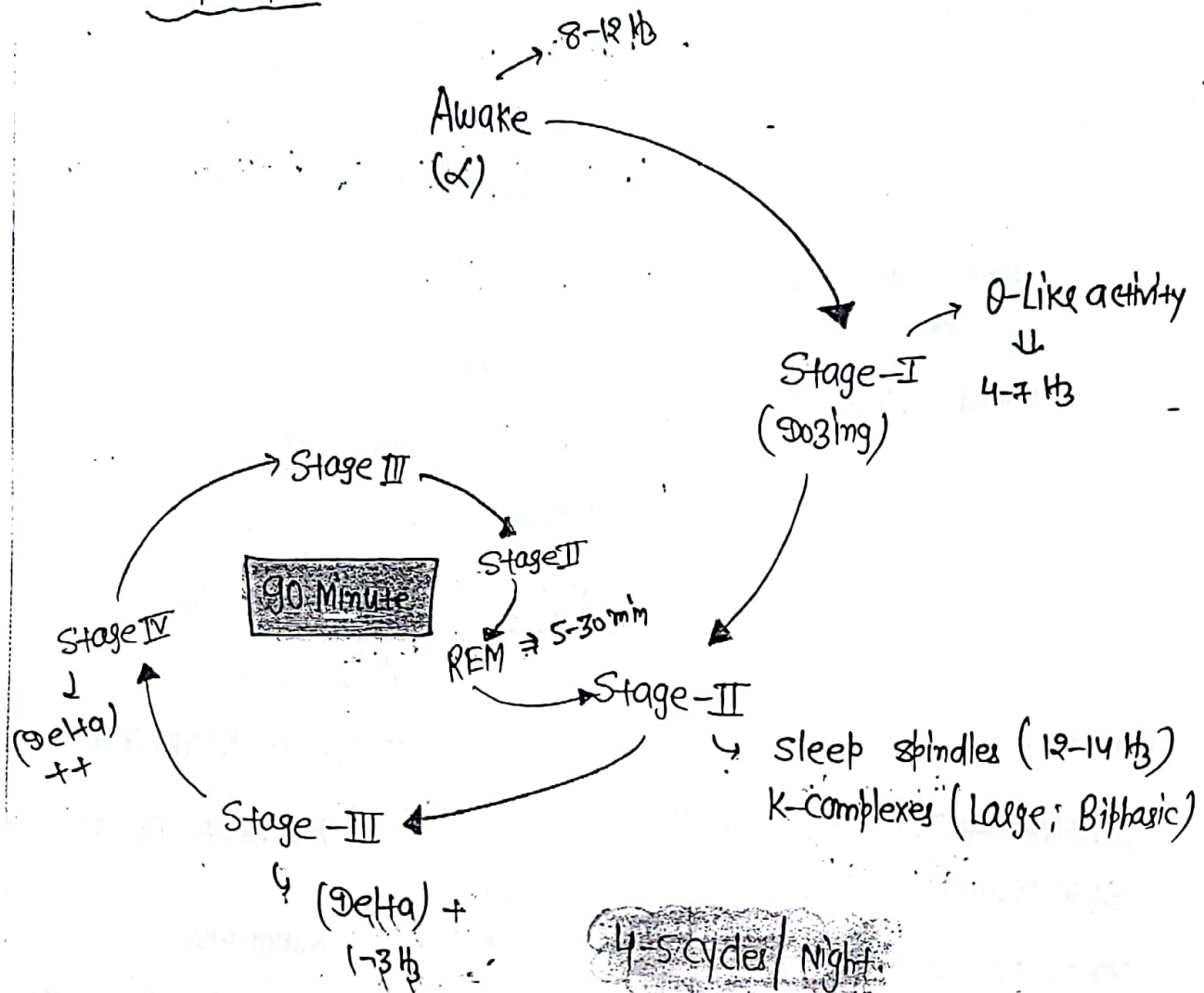
* Saw-tooth waves (Low voltage fast activity);

Reappearance of α -wave

* Tone of Neck Muscle is Markedly Reduced in REM sleep
(Other Muscles Retain their tone)

* Locus ceruleus Mediated Relative Paralysis \Rightarrow in REM sleep.

* Sleep cycle \Rightarrow



Most difficult to Arouse \Rightarrow Stage III & IV

\hookrightarrow Deep sleep or slow wave sleep; high Arousal threshold

* Total time spent in REM sleep \Rightarrow

Pre-term	\rightarrow	80% of Sleep time
Term	\rightarrow	50% "
Adults	\rightarrow	25% "
Elderly	\rightarrow	15% "

* On an average, REM sleep occupies 20-30% of Total sleep.
NREM sleep occupies 60-70% of Total sleep.

Time spent by different stages of NREM sleep →

Stage I ⇒	5-10%	} Total ⇒ $\frac{60-70\%}{\downarrow}$ NREM sleep.
Stage II ⇒	40-50%	
Stage III & IV ⇒	15-20%	

RAS (Reticular Activating System)

- ~~Ascending Polysynaptic Pathway~~
- ~~Non-specific system~~; which can be excited by ~~Any sensation~~
- on Arousal from sleep the EEG pattern changes to high frequency low voltage activity (β -wave) from high voltage slow wave (δ -wave) of sleep ⇒ "S-block"

*** Activation of RAS is Responsible for Arousal from sleep. **

